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PROCEDURES OF THE BLOOD BANK AT THE MASSACHUSETTS GENERAL HOSPITAL

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BOSTON

THIS paper is written to show how a large hospital, the Massachusetts General Hospital in Boston, set up its blood bank, met a variety of problems common to many such institutions, and finally evolved a practical system, the rules for which may be helpful to other hospitals, large and small.

SITE

Several important points require consideration in setting up a blood bank. The first of these is plenty of space. A good-sized bleeding room, not crowded and well ventilated, is pleasant for the donors and easier to work in. Separate rooms for blood storage and laboratory work are helpful, and a quiet recovery room is a great blessing. Overcrowding of laboratory workers in cramped quarters is a frequent cause for serious errors. A separate room for making plasma is useful, since freedom from air-borne bacteria is vital in avoiding contamination. The second consideration is availability to the operating room. Close proximity is advisable because transfusion is an operating-room procedure requiring some operating-room apparatus, a sterile technic and operating-room supervision. This is particularly true if the blood is to be stored or converted into plasma. Third, central location is helpful for blood distribution. Lastly, ready access to the front door of the hospital makes entrance easier for the donors and quieter for the hospital as a whole. A bank functions better with all its components — bleeding room, storage room and laboratory facilities — close together.

Plenty of space was obtained at the Massachusetts General Hospital in the form of four contiguous rooms with adjacent closets and sinks, as well as an adequate area for recovery beds. These rooms are near the front door, but are neither near the operating room nor centrally located and are at ground level — a disadvantage in a dusty city. The rooms are composed of a bleeding room, with a scrub sink and four tables for donors, a laboratory room, a blood-storage room, with space for physical examinations, and a room used only for the making of plasma.

APPARATUS

There are many useful types of apparatus on the market, put out by a variety of reliable firms. On the whole, bottles can be divided into refillable and dispensable bottles. The former are less expensive in those institutions in which it pays to run a solution room — that is, hospitals of at least 100 beds in which a well-trained staff can turn out parenteral fluids at a cost less than the price charged by commercial firms. The larger the hospital the greater is the saving; in some institutions the use of a solution room cuts the cost of fluids to twenty per cent of their market price. The Massachusetts General Hospital falls into this category and has for a long time used Fenwal flasks† for saline and dextrose solutions, as well as for blood, at a great saving. A partial vacuum can be obtained by sterilizing these flasks with their caps loosened, driving home the caps as the bottles come from the autoclave. This gives a vacuum of at least 95 per cent of the available flask volume. The number of flasks needed for working purposes is about four times the daily average of bloods expected to be stored. Thus, if forty bloods are usually on hand, one hundred and sixty flasks will provide for delays in cleaning and the slow return of flasks from the ward, and will furnish sterile sets ready for an emergency and enough flasks to carry a maximum load of eighty to a hundred bloods on hand at one time. As a matter of convenience a volume is maintained about six times the expected normal, which is a great help in a shorthanded hospital during wartime.

For storage, extremely well-insulated secondhand refrigerators were obtained, and the best new compressors were purchased to use with them. This was not only an economy but also an insurance against poor wartime refrigerator insulation, so frequently found in new iceboxes. The bottle-cooler type of refrigerator is used for the main storage. It

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†Obtainable from Macalaster Bicknell Company, Cambridge, Massachusetts.

possesses the advantages of easy access to the blood without moving flasks, and its temperature varies less than otherwise on opening the boxes, because they open from the top and, in the absence of a draft, hot air does not penetrate to the level of the blood. Two of these refrigerators were bought for the storage of blood after grouping, an upright box for ungrouped blood, typing serums and so forth and a box for plasma. Later there were purchased two more plasma boxes and another upright box to hold bloods waiting for plasma pooling and so forth. This gives an available storage space for one hundred and fifty to two hundred pints of whole blood and seven hundred pints of plasma. The last item of considerable expense was a large four-cup International centrifuge for use in separating both serum from cells and plasma from cells.

The other equipment bought consisted of the numerous adjuncts to transfusion such as a sterilizer, needles, tubing, syringes, trays, tables, desks, beds, bleeding tables, linen, an incubator, microscopes, printed cards, ultraviolet lights and curtains. In addition, the four rooms were partially rebuilt, cleaned and painted and about seven hundred refillable flasks were purchased for the storage of plasma.

The total bill for original equipment at the end of a year came to approximately $6500. This provided sufficient wherewithal to run a bank with a peak load of over five hundred and fifty transfusions of whole blood and two hundred of plasma for one month and with an ordinary load of 480 whole-blood and 60 plasma transfusions.

Personnel

The number of blood-bank personnel is partially dependent on the number of transfusions and partially on the complexity and careful detail with which the blood is handled; the type of personnel, however, cannot be so variable. A bank runs at its best only when the staff is well trained, able and permanent.

In the beginning, when planning for a volume of two hundred and fifty transfusions a month, we set up our staff so that all functions but physical examinations would be done by it. Later, however, an increased volume of business and a desire to provide some opportunity for all interns to learn the technic of blood collection led us to modify this position. There is a half-time director who is intimate with the working of the hospital services, particularly the surgical ones, which use 70 per cent of the blood; three nurses whose essential function is the drawing, storage and distribution of blood and pooling of plasma, one of whom is in charge of the bank (under the director); and two technicians whose primary functions are grouping and cross-matching but who can take blood or do any of the other work. Interns are used for assigned periods to do physical examinations on donors as well as to draw blood under supervision at set times. There are employed two medical students assigned for a year's duty, on call at night for emergency groupings and cross-matchings; two maids to clean glass and so forth; and, last but not least, a number of volunteer workers who fill out cards, look after the donors' welfare, and help out in a variety of other ways.

Finances

The original investment made by the hospital for the purchase of equipment was $5000. To this was added $1068 by the Office of Civilian Defense for the collection of plasma and about $500 from private contributions. The bank took nearly a year to spend this on original equipment and expenses exclusive of replacement of worn materials.

For maintaining revenue it was decided to charge $5 for the total service of taking the blood, grouping and cross-matching it, and administering it to the ward patients. Of this it was expected on the basis of present percentage of free service to collect but $2.25. For semiprivate patients the charge was $7.50 and for private patients $10. These charges, on the basis of a previous transfusion rate of thirty-two hundred a year, it was thought would maintain the bank. Owing to the fact that the rate of transfusions among ward patients increased by about 10 per cent, whereas that among private and semiprivate patients doubled, there was a larger income than expected, permitting expansion of the staff and the meeting of unforeseen expenses. Thus, it was possible to give more than one hundred and fifty plasma transfusions to the victims of the Cocoanut Grove fire (November, 1942), without charge, as well as frequent free transfusions. To patients who had no donors, the charge has been $25 for a pint of blood in addition to the service charge. At the end of the first year of operation (April 1, 1943) about $2000 had been paid back on the original capital, and there was a small reserve and in addition a sum of money on hand for buying blood when necessary — called the "Blood Bank Replacement Fund." It works as follows: The money collected from patients for the purchase of blood — that is, from those patients who have no donors and therefore pay $25 for each pint of blood — goes into the fund, and all money paid to the professional donors comes out of it. When the private and semiprivate patients were taken over after two months of operation, it was quickly found that most of them preferred professional donors to family ones, particularly if the patients came from a distance. To cancel the service charge in whole or in part in return for voluntary donors' furnishing more blood than was needed, as has been done elsewhere, was thought to be hazardous to solvency and an insufficient inducement to most patients because the charge is fairly low. Instead, $1000 was borrowed from the hospital with which to purchase blood to replace that given to these patients. This meant that we not only sat-

isfied the professional donors but also could call in donors at any time when the supply of blood of a particular group was too low. Soon this side of the business increased because one third of the transfusions were among the private or semiprivate patients. Because of available voluntary donors, the entire fund was never used; recently, because of a shortage of professional donors owing to the demands of war work, it has also grown so that there is now about $5000 on hand. This fund is most useful for patients who require fresh blood; they send in their voluntary donors at any time, and a professional donor is sent for at the time the transfusions are requested, fresh blood being furnished at no extra charge. To keep up the supply of Rh— bloods, these are purchased from the donor list or the Blood Grouping Laboratory (Children's Hospital, Boston). Before holidays or at any time when extra bloods of a given group are needed, professional donors are sent for and a supply is laid in.

System of Credits and Debits

Most fundamental to adequate service in a blood bank is a constant stream of donors well in excess of needs. Many banks have run into serious difficulties because of neglecting this simple truth. For each hospital the problem is different. Prior to the establishment of our bank, we had plenty of available voluntary donors, so that no shortage was anticipated on beginning operation.

System of Patients' Credits

To keep up a larger volume of deposits than of withdrawals, it was requested that for each transfusion two or three bloods be deposited in the bank. Furthermore, no blood is allowed to be issued to a patient who has no deposits on hand unless there is a guarantee of cash replacement. To enforce this, if the patient has no credit, permission for transfusion must be obtained from one of the hospital directors. The directors are moderately severe in enforcing this provision, with the result that neither the hospital staff nor the patients do much sidestepping of obligations. The necessity for this is obvious. In the first place, the patients' families rarely replace bloods already received; in the second place, it is difficult for a blood-bank nurse to refuse to issue blood to a physician, whereas a director can readily do so if he thinks that little or no effort has been made to obtain donors. In worthy cases where there is no credit, the director's permission is given by his signature on the requisition. This permission is given freely, and by telephone in emergencies. To keep track of the patient's credit, a card file is maintained in the bank, listing for each patient the number of donations of usable blood and the number of withdrawals for actual use. Blood withdrawn from the bank but not given, as happens occasionally, is as a rule, charged to the patient, although in certain cases the bank has accepted the loss. On the wards, the intern staff follows the patient's debit and credit on a deposit and withdrawal form marked with a rubber stamp. All this is complicated, but it actually saves both labor and disputes and provides a wise safeguard against profligate withdrawals.

Bloods do not expire with the passage of time on a patient's credit slip unless the patient leaves the hospital for a month or so. This is only fair, since blood costs the patient money and takes time and trouble to obtain. The blood bank loses nothing by permitting this or by relaxing its policy of maintaining credit beyond a month of absence in isolated cases. As a rule, the volume of blood coming in amply covers withdrawals, regardless of when the initial deposits were made.

Service Credit

The record of credit or debit of the different services or divisions of the hospital is to the blood bank what a balance sheet is to commercial banks with this fundamental difference: Good service can be provided only if there are ample amounts of four forms of currency, — that is, the four blood groups, — whereas commercial banks deal with only one form. Furthermore, two of the groups, Types B and AB, are rare. To be sure, to have enough blood on hand to care for a bleeding peptic ulcer in a Type AB patient a minimum of sixty bloods of all types must be on hand; in actual practice a minimum of eighty to one hundred is generally safer. Although there is no hesitation in using a carefully cross-matched universal donor's blood from a repeatedly typed professional donor in an emergency, or in switching to the original type after a fresh blood has been taken from a patient for cross-matching, it is still preferred to administer a blood of the same group as the recipient's and an effort is therefore made to keep bloods as close to the one-hundred mark as possible.

In keeping to this standard, which is often difficult, the system of service credit is regarded as the most important factor. Under this system, the actual number of usable deposits made to the credit of a service — that is, by the donors for patients on a service — is recorded on a blackboard, and from this are subtracted the bloods used by that service or belonging to it and expiring unused at the end of seven days. No credit is given for a blood of small quantity or with a positive serologic test or one that is considered otherwise unusable. This credit is much more real than the patient credit, for it represents actual blood on hand, less, of course, blood given out to the patients paying cash and for whom professional donors have not yet been purchased. Thus, when a blood is deposited for one of the surgical services but is actually given to a private patient who pays for it, it is listed to the credit of the surgical service long after it has actually been used; at the same time the debit for this

blood is listed in the debit column under "professional donors." On each occasion when professional donors are sent for, the bloods used are subtracted from the debit column, the service not losing credit until a blood is actually given to its patient. This system is obviously open to criticism on the ground that the service credits of all services minus the debit for professional donors not yet sent for could readily equal zero and there would be no blood in the bank. To prevent this from occurring, a careful check is kept of bloods of all groups actually in the bank with an eye to preventing depletion. The number of bloods has on occasion gone as low as eight and as high as one hundred and thirty, but as a rule an average of sixty bloods is maintained, which cares for sixteen transfusions a day.

The enforcement of this system is, however, no less important than is the understanding of its functions. A credit is insisted on at all times. Although the issuance of bloods to a patient with credit is continued when the service has none, — and out of all fairness to patients, there could be no other course,— the responsibility for the debit is placed on the head intern or resident of the service involved. He is warned by the nurse in charge of the bank when his credit is low. How low it is depends on the volume of blood used, for the general surgical services, a low level is considered to be 6000 cc., because sick patients may exhaust this supply in a few days, whereas for the Dermatological Service a credit above 1000 cc. is considered high. A debit calls for admonition from the bank director to the resident. A lack of response is usually followed by an appeal to the chief of service by the bank director, and as a last resort, the director of the hospital is informed of the situation. It is rare that any person above the house staff has to be appealed to. This is only true because the co-operation of the chiefs of service and the support of the hospital director can be relied on. This system will only work in well-co-ordinated private hospitals.

When patients are transferred from one service to another, their credit goes with them. This works a hardship on the medical services but is on the whole fair, because the preoperative use of blood is equaled or exceeded by its operative or postoperative use; if credits remained stationary, the surgical services would often be unfairly in debt. Expiration of blood, causing a debit, is a great hardship; unfortunately, the only method of compensating for it is to maintain a great excess of donors over transfusions (high service credit). The benefit of expiration is that it means plenty of plasma for therapeutic or research purposes.

Care of Donors

It is the responsibility of the doctor in charge of a patient to send for donors well in advance of the time needed. This responsibility sometimes devolves on a nurse at the Information Desk. This means that the patient's relatives frequently receive a slip of paper telling of banking hours and the rules about diseases and the taking of alcohol and food. If they are infrequent visitors to the hospital, they receive a telephone call, telegram or letter. The bank is open five afternoons a week, two evenings until 7 p.m., and on Saturday mornings. Tuesday afternoon is the only time for receiving donors by appointment, the reason being that many speak too little English and that others come from too long distances to keep exact dates. An attempt is made to receive donors for private patients or volunteer donors on Tuesday afternoons. Evenings are popular for war workers. Saturday afternoon and Sunday would be popular times for donors, but since attendance of the entire bank staff would be required they are avoided.

An effort is made to have donors looked after so far as possible by a volunteer worker, who makes out their cards, supervises their signing a release (these are needed in most states), and provides them with magazines and so forth while they are waiting. A history regarding contagious, debilitating and allergic diseases is taken, also the hour of last eating, alcohol ingestion, and the time of the last donation of blood. The history-taking and a brief physical examination, including the heart, the respiratory system, the blood pressure, the lymph nodes and, for males, the genitalia, are done by an intern. A blood smear is made and the hemoglobin and the temperature are determined by a technician. Donors are rejected if they have had transmissible, recent or debilitating diseases, are allergic, have eaten within the last four hours, or have taken alcohol within the last twelve hours. Abnormal blood smears and positive serologic reactions are cause for the discarding of blood. The main objection to recent eating lies in the elements of the donor's diet to which the patient is sensitive. This is also true of certain alcoholic beverages, but on the whole the main objection to the donor who has been drinking is lack of co-operation and frequent vasomotor collapse after phlebotomy. Donors of eighteen to seventy years of age are accepted outright, those under twenty-one years only with the permission of their families, and those over fifty-five only if in excellent condition, particularly so far as cardiac and peripheral vascular systems are concerned. Women weighing less than 100 pounds are usually rejected. On request of their physicians, patients with polycythemia, hypertension or decompensation are accepted as donors, but the blood of those with polycythemia is usually discarded, since it is too viscous to run freely. In a year's operation, between 16 and 20 per cent of donors were rejected on the ground that the giving of blood would be harmful to them or, more often, that their blood would be of poor quality or harmful to the patients.

When a donor is ready for phlebotomy, the outer clothing is removed and a clean gown and mask are put on. The donor is led into the bleeding room, where curtains are drawn between the tables so that he sees no blood being drawn. We do not agree with certain other bleeding centers that the observation of others being bled exerts no psychological effect or that, if it does, the effect is a beneficial one. We believe that the contrary is true, and our rate of syncope during phlebotomy is almost negligible. After termination of the procedure, the donor lies for five to ten minutes on the table, which is cushioned and soft; he is then escorted to a bed on low shock blocks in the recovery section, where milk, peanut butter and crackers are given. After a minimum of twenty minutes' rest, or longer if there is any feeling of faintness, the donor dresses and leaves the hospital. There have been rare cases of collapse after leaving the bank, but almost without exception these have occurred among donors who failed to follow the rules. Donors are sent cards giving their blood group and the date of donation, with room for more dates to be added.

FIGURE 1. *The Blood-Withdrawing Set with Filter in Place.*

THE TAKING OF BLOOD

The bleeding of a donor is regarded as an operating-room procedure and is carried out with complete sterile technic throughout. Under this system, the number of contaminated plasmas has been extremely low, so that it seems to be justified. The entire recipient set is autoclaved in heavy wrappings and is generally used within forty-eight hours of preparation. Great care is taken to clean all apparatus immediately after use, particularly needles and tubing, which are washed with a high-speed water jet and soaked in N/10 sodium hydroxide, followed by thorough rinsing. The nurses who use the needles sharpen them on an electric grindstone, an important point in all intravenous work. The system of blood collection is a closed one operating by gravity instead of a vacuum — that is, there is an outlet on the head of the flask to permit the exit of air. A cotton air filter is inserted in the outlet to prevent contamination of the set by the entrance of air as the bottle cools after sterilization, or as air goes in and out with changes of room temperature and atmosphere pressure. These sets work well and are simple to operate. If the blood flow is slow, an Abbott suction bulb may be attached to the filter. Sixty centimeters of a 4 per cent solution of sodium citrate is used as an anticoagulant. The unnecessarily large amount is advantageous in preventing clots toward the end of the procedure or if more than 500 cc. of blood has inadvertently been drawn. This procedure has not increased hemolysis. Bacteriologic culture medium is inserted in the sets from time to time to check the effectiveness of sterilization.

The nurse taking the blood wears operating-room clothes and is gowned, scrubbed and gloved. The donor's arm is prepared for her by a nonsterile assistant with ether and then iodine. The needle (a No. 14 steel cannula with a glass adapter) is inserted through a novocain wheal without incision. The adapter gives prompt visual evidence of venipuncture. Only two tries are made on a donor, one on each arm, unless he is insistent on further ones. At the termination of the procedure, the tubing is clamped immediately above the flask on both the intake and outlet and cut. Blood for a Wassermann

test, blood grouping or determining the Rh factor is collected in two test tubes. The blood in the flask is agitated throughout the procedure and for half a minute afterward, since the anticoagulant is extremely diluted at the end, requiring extra shaking. The blood is allowed to cool to room temperature for half an hour before refrigerating, since slow cooling lessens hemolysis. The flask and its test tubes are labeled with the donor's number before they leave his side.

Blood Storage

Prior to the Wassermann report and the completion of grouping, bloods are stored by number in the laboratory refrigerator. As soon as they are ready, they are tagged with labels of different colors for the different groups and marked with the date, the donor's name and number, the Wassermann reaction and the name of the person who did the typing. They are placed in separate compartments in the bottle coolers, which are marked and colored similarly to their tags — O, A, B and AB, respectively. The donor's card, after it has been stamped to show the blood type, the Rh factor and the initials of the persons doing the grouping, is filed in a box colored and labeled similarly to the refrigerator, the cards for the oldest bloods being at the front of the box. Furthermore, this and all other information, including the person and service for whom the blood was given, is recorded in the bank book. This is an elaborate system, but an almost foolproof one so far as errors are concerned — donors' bloods are clearly separated and marked for type by letter, by color and by compartment; so also are the donors' cards. The bank book record acts as a check.

The temperature of the refrigerators and bottle coolers is kept at about 39°F. by means of thermostatic control. Prevention of a wide variation in temperature is carried out through the medium of thermometer dials on the outside of the boxes and an electric alarm system connected to the Maintenance Department, where there is someone on duty night and day. The compressors are set apart from the refrigerators to prevent agitation.

After a whole blood has reached the seven-day expiration date, it is placed in another refrigerator for conversion into plasma. The donors' cards and the bottle tags are filed after the expiration dates and disposal of the bloods have been recorded on them.

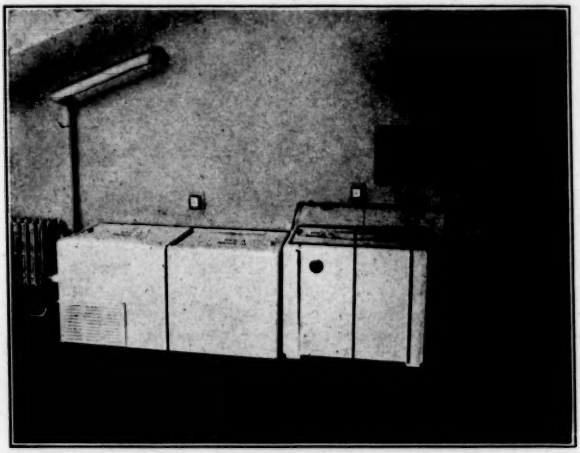

Figure 2. *The Bottle Coolers Used for Blood Storage.*

System of Blood Grouping and Cross-Matching

The hospital changed from the Moss to the International system of blood-type nomenclature with the opening of the bank. At the same time, there was inaugurated a careful system of double checking of all groupings and cross-matchings by having each checked by a different person. This is helpful with difficult typings and avoids the mechanical errors of using wrong test tubes and so forth. Types O, A and B testing serums are used, each one being a pooled serum obtained from three high-titer donors. The blood cells to be tested are prepared in a 2 per cent saline suspension prior to being intro-

duced into the known serums on a slide. Lecithin is placed on one slide for each grouping to prevent rouleau formation, twenty minutes in a Petri dish — to prevent evaporation — being the time required for maximum agglutination; all slides are then read under a microscope. In the rare cases in which a very sick patient or one who has had a large amount of sulfonamides is difficult to group, an incubated cross-matching is done with a thoroughly well-known — usually professional — universal donor. In not only insisting on the system of double checking all cross-matchings and groupings but in having them done by the bank staff in so far as possible, a great measure of safety is provided, for diversification of responsibility carries the procedures into unskilled and often careless hands. An intern must have seen severe reactions in addition to possessing some knowledge of subgroups, cold agglutinins and so forth, to be able to conduct himself adequately in a blood-grouping laboratory. This is why medical students are trained to do the work at night, their work being checked by someone high up on the service — a person of known ability certified by the bank. When staff members are not present, in place of grouping and matching of the patient's blood in an emergency late at night a carefully cross-matched blood from an Rh— universal donor is used. In an extreme emergency brooking no delay, a known universal Rh— blood can be given out without cross-matching with some degree of safety. This is practically never done, since cross-matching or the use of liquid plasma is preferred for these cases.

High-titer Rh-testing serum of high specificity and stability is purchased from either the Blood Grouping Laboratory or, more rarely, Dr. Philip Levine, of Newark, New Jersey, and with it all donors are tested. A test is also done with all patients requiring multiple transfusions or having a history of reactions, miscarriages and so forth. Dr. Levine's[1, 2] method is employed for these determinations. Cross-matchings are frequently incubated for an hour, particularly if patients have had severe reactions from Rh+ blood although positive themselves, or if they are first tested after receiving several transfusions. The charges for Rh testing are $2, $3 or $4 for ward, semiprivate and private patients, respectively. An average of twenty testings are performed each day, excluding Sundays and holidays.

FIGURE 3. *The Pooling of Plasma.*
The bloods to be used are on the left. Plasma is running into the pooling flask. On the extreme right are two flasks containing diluent and ready to be filled with plasma.

PREPARATION AND STORAGE OF PLASMA

Ninety-five per cent of the plasma is drawn from bloods beyond the seven-day expiration date, and 5 per cent of it from volunteer donations. The plasma is pooled whenever there is sufficient blood on hand to do so, usually two or three times a week. The centrifuge is useful only with bloods under three days old; after that time, the cells are too fragile to withstand the 20°F. rise in temperature and concomitant agitation of fifteen minutes of spinning, which causes over one third of the bloods to show some degree of hemolysis. On certain occasions, as with the large influx of voluntary donors after the Cocoanut Grove fire, the yield was increased from 70 units of plasma per one hundred flasks of whole blood to 95 units by centrifuging twenty-four-hour-old blood. To make a pool, blood is selected from

all groups if possible, and never from Group O or A alone.

Prior to pooling, the air in the plasma room is sterilized by two hours of ultraviolet radiation, after which there is as little commotion and introduction of outside air as possible. The pooling of plasma is carried out as a completely sterile procedure with the workers capped, masked and in clean clothes. The operator prepares as for an operation, wearing a sterile gown and gloves. The supernatant plasma is drawn off by a needle inserted through the tubing on the bottle top, which has been previously sterilized by soaking for twenty minutes in 1 to 1000 solution of mercury bichloride. The needle is connected to a 2000-cc. pooling flask from which the air has been evacuated. As the plasma is drawn off, it is replaced by room air through a sterile air filter. When the pooling flask is full, it is agitated and can then be cultured immediately, or it may be left undisturbed for a few days and then cultured.

Culturing, carried out according to the rules of the Office of Civilian Defense,[3] is done by inserting 10 cc. of plasma deep in each of four test tubes containing 20 cc. of the aerobic-anaerobic Brewer's medium (thioglycolate broth). The pool is then drawn off into plasma flasks with a fresh needle, after which the cap and needle are removed and a permanent metal cap is put in place. The flasks contain either 250 cc. of normal saline solution or 50 cc. of 50 per cent glucose solution, freshly prepared and autoclaved. They are usually frozen immediately at −30°F. to reduce fibrin and fibrinogen-clot formation, and are stored at −10°F. or kept at room temperature. As a rule, the plasma is drawn from the pooling flasks into the final containers, a residual being left at room temperature for a day before culturing. This saves one motion and makes for one less introduction of a needle through the flask top.

Two of the culture tubes stand for a week at room temperature and two in an incubator. If two or more are contaminated, the entire pool is discarded. If one is contaminated, reculturing is done; if there is no growth the pool is used, on the theory that the original culture tube became contaminated; if there is growth it is discarded. The use of separate needles for each flask of blood or plasma, the keeping of all apparatus covered when not in use and rigid rules of preparation of sets and bottle tops (the former are autoclaved) reduces contamination.

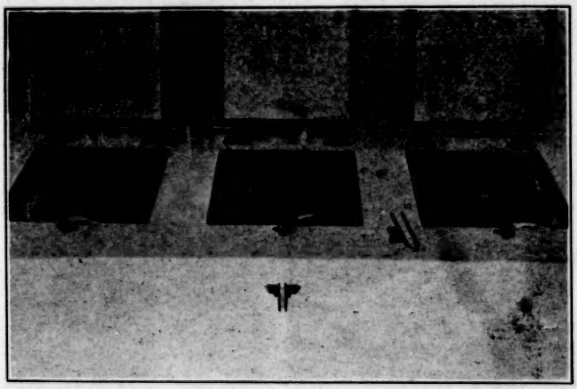

FIGURE 4. *Plasma Storage Box.*
The section on the left is maintained at −30°F. for quick-freezing purposes.

It has been found that connecting water suction to the flask, if the vacuum is exhausted, leads to air leaks in the connections of the set. This suction method was instituted just before the ultraviolet lights were installed, and immediately four pools of plasma were found to be contaminated. On using the lights and changing nothing else in the technic this contamination ceased. The studies on the effect of ultraviolet radiation in reducing the bacteria in room air are not complete. Exclusive of these four pools, the percentage of contamination in the making of over twelve hundred flasks of plasma is under three per cent.

We consider a plasma diluent advantageous because it cuts down on fibrin and fibrinogen-clot formation and permits much better flowing through both the filter and needle, since plasma is viscous. It also helps to prevent agglutination of the recipients' blood cells by the action of powerful anti-A or anti-B agglutinins in the plasma. Saline solution is the better of the two diluents for mechanical reasons, but may be dangerous, because of an overdosage of salt, if more than six transfusions of

plasma so diluted are given in twenty-four hours. No mercurial preservative is used because in sterile plasma no antiseptic is necessary, because the preservatives now advocated (except sulfathiazole) are poor bactericidal or even bacteriostatic agents, and because there is danger of mercurial damage to the kidneys in the use of large volumes of plasma so treated. This damage has been proved to exist, since 2 patients dying of other causes showed it at autopsy.

Most of the plasma after quick freezing is stored in thermostatically controlled refrigerators at −10°F., protected by electric thermometers and an alarm system. Some plasma is kept at room temperature and some, diluted with saline solution, is stored in the refrigerator. Both are ready for immediate use after negative cultures, and are useful for emergencies. We have distributed plasma to other hospitals for storage, and are equipped to give out to any hospital plasma in Fenwal flasks, with sterile glass vent tubes and rubber tubing ready for connecting to intravenous apparatus.

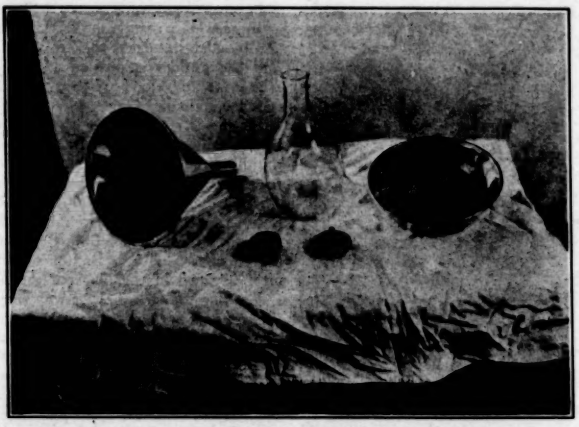

FIGURE 5. *The Sterile Filtering Set.*
On the right is the fine-mesh stainless-steel sieve; on the left, the stainless-steel funnel.

ADMINISTRATION OF BLOOD AND PLASMA

In requisitioning blood or plasma the physician fills out a requisition with the patient's name, number, ward, diagnosis, reason for wanting blood or plasma and the time it is wanted — usually twenty-four hours in advance — except in emergencies. This form, accompanied by 5 cc. of the patient's blood, arrives in the bank; the patient is then grouped by two persons and the oldest blood of that group on hand — on the average three days old — is selected, two cross-matchings are done, and the blood is set aside ready for use. In an emergency, if an Rh typing has not been done on the patient, an attempt is made to give an Rh− blood or plasma, but we deplore unnecessary emergencies, preferring to set up bloods unnecessarily a day ahead rather than to try to do important laboratory work in a hurry at the expense of routine work. In case a blood is not called for at the time specified, the ward is called, and if the patient does not need it, it can be used for someone else, since it has not left the refrigerator.

There are two means of preventing blood from being given to the wrong patient. The first is to have the person who is to make the transfusion come and get it, checking its tag, which has already been marked with the patient's name; the second is to let such a person take only the blood for one patient at a time. The medical services have a wise additional safeguard in the form of still another cross-matching done by the intern at the patient's bedside.

Just before the blood is given out, it is filtered through a stainless steel sieve, 14 cm. in diameter with a 0.2-mm. mesh in its bottom. It rests in a stainless steel funnel set in a flask. The whole has been autoclaved and the sieve moistened with saline solution to break the surface tension. This eliminates both large and irregular filters such as gauze or beads, or the Baxter and Cutter filter drips, which are excellent for filtering but altogether too frequently cause a reduction or stoppage of blood flow. If the blood is used immediately, the chance of the formation of a fresh plasma or blood clot is negligible. Forty-eight of these sets are kept on hand, a number well in excess of any day's transfusions.

When the blood arrives at the patient's bedside, the person administering it is supposed to check its tag with the patient's name, particularly if a nurse brought the blood from the bank. There has been some difficulty due to bloods' being improperly handled — that is, either they have been heated by some misinformed person, or after being exposed to room air in the filtering process they have been put in a ward refrigerator for a few days. Since these practices promote bacterial growth and hemolysis, we have attempted by education to eliminate them.

The fluids are administered on the private and semiprivate wards by two nurses specially trained in

FIGURE 6. *The Administration of Whole Blood After Filtering. Note the flask of saline on the table with which the infusion was started by the intern.*

intravenous work and on the general wards by interns. This use of nurses, started as a war measure, has proved to be highly satisfactory. They can be taught a single dependable method of therapy, after learning which there is no shift to new ideas and no deviation from accepted standards of safety. Interns have been retained as fluid administrators on the wards because of the value of their learning the fundamentals of needle insertion and intravenous therapy. The nurses sharpen their own needles. They are taught to begin all intravenous administration with a saline or glucose solution and after the fluid is running well, to shift to blood or plasma. This saves both material and veins. They use, except in emergencies, the most peripheral veins first (usually those on the hand) with careful splinting of the part and good sterile technic. They are taught always to feel for the radial pulse after application of a tourniquet. The antecubital veins are avoided in case the patient should have a protracted illness. We do not hesitate to use and have found to be satisfactory the sternal route of fluid administration. All persons, interns and nurses, are instructed in these measures and are told to sit with all patients having transfusions for the first five minutes of running, because within that time the warning of a fatal reaction usually appears. At the end of the transfusion the card attached to the bottle neck is filled out as to reaction, blood flow and so forth and returned to the bank. One per cent to 2 per cent of these cards are not returned, but by pressure being kept on the head ward nurses they are usually sent in.

In case of a reaction, the transfusion is stopped, the blood is returned to the bank for regrouping, and the patient is put on an alkalinizing regime. The urine and blood are subsequently examined for free hemoglobin.

Plasma is requisitioned similarly to whole blood, but its administration is different. It is melted in a rapidly circulating water bath at body temperature regulated by hand and checked by a thermometer. There are, however, special metal racks for the purpose of melting thirty-two units at a time in case of disaster. Plasma is administered through an intravenous set with a Baxter or fine-mesh Cutter filter inserted in the place of the usual drip bulb. Below the filter lies a three-way stopcock to permit the use of a syringe for rapid administration. This system works well; there is little clot and no stoppage of flow due to it. Furthermore, it is certain that there will be no trouble from minute pulmonary infarcts. Shortly after the inauguration of the bank, we began to use these filters on the commercial dried plasma then being administered in the hospital and cut the reactions down from a fair degree of frequency to a rare one. There are one hundred sterile filter sets on hand at all times in case of civilian disaster, such as a fire or a bombing.

There is a charge of $25 for the plasma, the same as for blood, but we are far more liberal in giving it out to patients who can neither replace it nor repay us. This is done because plasma is considered in large measure a byproduct. In case of disaster its administration is given free.

Records and Reactions

The tags on the plasma and whole-blood flasks give the final record of what happened to the blood and are filed with the donors' cards. From time to time there are brought up to date the number of rejected donors and the reasons for rejection, the number of bloods used for plasma, the whole bloods given and the reactions. An attempt is made to find the reason for the reaction in each case, particularly in serious ones; for this purpose the facilities of the Blood Grouping Laboratory are available. To date, the percentage of reactions since the installation of

the metal sieves has remained constant at 6.3 per cent. This includes 1.2 per cent of serious reactions as evidenced by high fever and chill, 1.5 per cent of minor chill and temperature reactions probably due to foreign matter in needles, bottles or tubing, 2.6 per cent explicable on an anaphylactic basis, and 1 per cent of a vague class of complaints, many of which are coincidental with, rather than caused by, transfusion. These figures are based on the first four thousand transfusions after a preliminary survey. There was 1 patient with serious post-transfusional oliguria who died on the operating table. This was thought to be a case of an anti-Rh hemolytic reaction. The death occurred prior to the present system of Rh determinations.

Conclusion

The methods and rules used by the blood bank of the Massachusetts General Hospital have been derived partly from the experiences of others and partly from our own experiences. They form a workable system that may, and we hope will, help other hospitals to set up blood banks or to iron out the many difficulties into which such institutions run.

References

1. Levine, P., Burnham, L., Katzin, E. M., and Vogel, P. The role of iso-immunization in pathogenesis of erythroblastosis fetalis. *Am. J. Obst. & Gynec.* 42:925-937, 1941.
2. Levine, P. Personal communication.
3. Medical Division, Office of Civilian Defense. *Blood Plasma.* Technical Manuals. Supp. No. 1. 10 pp. Washington, D. C.: Goverament Printing Office, 1942.

DIET IN PREGNANCY

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WARTIME rationing of foods and the difficulties encountered in purchasing a selection of unrationed foodstuffs present a serious problem from the nutritional standpoint to the pregnant woman and her developing fetus. Various surveys[1, 2] in the past have shown relative dietary deficiencies directly paralleling economic status, but the present emergency places all women in the same category. The relation between the pregnant woman and the fetus is one of aggressive parasitism on the part of the latter, all its requirements being taken from the maternal organism. Eugenically the parturient state calls for the very best, from a nutritional standpoint, that the civilized state can present, so that the growing fetus will have available the maximum and optimum material essential to assure generations free from anomalous deficiencies of growth, as in the teeth, female pelvis and so forth, without extracting too great a toll from the parent host. It is the responsibility of the physician conducting prenatal care to make every effort to ensure the physical stamina and constitutional adequacy of the newborn infant.

The well-defined clinical syndromes of specific dietary deficiencies are too well known to require elaboration and are not common in obstetrics, although occasionally reported in the literature.[3] The vast majority of deficient nutritional states, however, do not reach levels productive of a clinical syndrome, but rather present a myriad of bizarre complaints that too often are dismissed by the attending physician with a mild sedative or explained away on a psychoneurotic basis. Thus, in 84 per cent of cases Williams and Fralin[4] found that such common complaints as nausea and vomiting of early pregnancy and easy fatigability, numbness and muscle spasm in late pregnancy were associated with below-standard consumption of vitamin B.

It is generally agreed that the average pregnant woman engaged in domestic affairs requires approximately 2500 calories a day to carry on her increased metabolic activities.[4, 5] This figure varies between 2000 and 3000 calories for the average woman of one hundred and twenty to one hundred and fifty pounds, depending on the state of her nutrition at the onset of pregnancy. Thus, although in the vast majority of cases it is prudent to restrict weight gain during pregnancy to 20 to 25 pounds, some women prior to conception are below average minimal standards for height and weight, and in them the parturient state with its general enhancement of metabolic activity and relief of psychoneurotic tension brings about an opportunity to correct long-standing imbalance between height and weight. The reverse is of course true in obese women, and their diets should be accordingly restricted from a caloric standpoint. Studies by Waters[6] indicate that a weight gain of over 22 pounds is retained post partum in 60 to 80 per cent of cases, except in hydropic patients. It is of course important to distinguish carefully between hydropic and stereoplastic weight gain, both from the dietary viewpoint and from that of active prophylaxis against impending toxemia. The growth of the fetus is parasitic, and most obstetricians believe that the weight of the fetus cannot be controlled by that of the mother unless the latter be placed on starvation rations. Adair[7] and others found the growth of the fetus to be independent of the intake of fats and carbohydrates if the total calories were adequate. Intrauterine deficiencies affecting the fetus—for example, rickets—may be produced by starvation and depletion of maternal mineral reserves, as pointed out by Maxwell, Hu and Turnbull,[8] Rector[9] and

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others. Sontag[10] believes that scurvy tends to appear early and in a malignant form in children whose mothers suffer from vitamin deficiencies.

Attempts have been made to correlate deficient diets with the major and minor complaints of pregnancy, with results that are not conclusive at this time. Ebbs et al.[11] found a high incidence of miscarriage, stillbirths, prematurity and minor complications in pregnant women on deficient diets, but Williams and Fralin[1] were unable to find a direct correlation, admitting, however, that such defects might not be present until a later date when the full histories of the child and mother were available.

The essential elements in an obstetric diet are protein, fats, carbohydrates, calcium, phosphorus, iron, iodine and the vitamins. With adequate amounts of these elements all the requirements will be adequately met. Furthermore, the use of sodium chloride should be restricted.

Protein. Protein, both animal and vegetable, in quantities of 80 to 100 gm. daily, is at long last recognized as an essential for the obstetric patient. In the past, fear of kidney complications or the presence of kidney disease has caused a restriction in protein consumption, with a resultant deficiency syndrome of anemia, loss of muscle tone, edema and lowered resistance. In late pregnancy the maternal organism stores over 100 gm. of protein daily in anticipation of labor and lactation.

Fats. These are also required in quantities of 80 to 100 gm. daily and are utilized primarily for energy and for enhancing the utilization of vitamins.

Carbohydrate. This is the basic food element that allows the greatest latitude in varying consumption to control adequate caloric intake. It is estimated that 100 to 300 gm. daily is necessary to provide energy for the mother and easily assimilable food for the fetus. Whereas protein consumption may be placed at a minimal level to assure the essential elements, carbohydrate intake may be varied to suit the caloric requirement in relation to excessive weight gain. Carbohydrates are the most easily obtained foodstuffs in rationed and wartime diets, and therefore may easily assume too great a percentage of the total caloric intake. This is important, as pointed out by Becker et al.,[12] since increased amounts of thiamine chloride are necessary when the carbohydrate content of the diet is raised.

Calcium and phosphorus. Calcium intake in pregnancy should attain levels of 1.5 to 2.0 gm. daily. The calcium-phosphorus ratio and metabolism are extremely important, and failure to maintain them at desired levels leads to complaints of cramps, insomnia and headaches. Deposition of calcium in the fetal bones begins at the fourth month and continues to term, with increased demands from the seventh month on, so that at term the fetus contains approximately 24 gm. of calcium.[13] Dental authorities do not believe that this demand on the mother is productive of tooth decay, as was formerly thought, but it is recognized that marked calcium deficiency may lead to postpartum hemorrhage due to uterine atony. Hart and Noble[14] advocate the intravenous use of calcium in such situations.

Iron. The daily requirement of iron varies between 20 and 30 mg., depending on the state of the blood at the time of conception. It has been shown by Hunscher[15] that hemoglobin levels parallel adequacy of iron in the diet. The relative amount present in the maternal organism varies with changing fluid levels, but it is known that at term the placenta and fetus contain approximately 900 mg. of iron, so that the absolute demand is constant.

Iodine. In this part of the country one need not be concerned with the intake of iodine as in endemic-goiter belts, but the intake may be assured by the use of iodized table salt in selected cases.

Vitamins. The daily requirements of the vitamins are difficult to determine because of the multiplicity of their effects on the human organism. They are estimated on the basis of the smallest amount that will prevent visible and recognizable symptoms of deficiency, with an added safety factor to cover individual variations. Vitamin A is important to promote growth and fertility and for the maintenance of epithelial tissue. Its effect on visual purple is well known. It is estimated that 6000 to 9000 international units is required daily. Chief among the requirements of the vitamin B complex is that of thiamine chloride, and its adequate intake will ensure the intake of sufficient amounts of the remainder of the complex. Insufficiency of thiamine chloride is known to cause undue fatigue, loss of appetite and other gastrointestinal upsets, headaches and mild neuritis. The importance of this vitamin concerns every cell in the body rather than any one organ or system. The daily requirement varies between 1.0 and 1.8 mg. of thiamine chloride. Vitamin C requirements are met by an intake of 1500 international units or 50 to 100 mg. of ascorbic acid daily. Vitamin C is concerned with the cementing of intracellular material, and deficiencies are manifest in clinical and subclinical scurvy, the teeth, lack of resistance to infection and predisposition to brain hemorrhage in the fetus. Ley[18] states that vitamin C stimulates the production of corpus luteum hormone. Vitamin D regulates the utilization of calcium and phosphorus. The daily requirement varies between 600 or 1000 international units.

Sodium. The sodium balance in pregnancy is usually positive and more than adequate for fetal needs. Restriction of sodium chloride is advisable; there should at least be limitation of its use to cooking, with absolute prohibition of its use at table. This is advisable both because of its relation to fluid retention and toxemia and because, as pointed out by Wadlow[16] and Pomerance and Daichman,[17] depletion of maternal salt leads to a shorter and easier labor, probably owing to dehydration of the cervix and uterus, leading to more efficient and effective contractions.

With an understanding of the requirements of the maternal organism and the demands made on it by the growing fetus, one can appreciate the fact that the one variable concerned is the total caloric intake. Rationing and the difficulty of securing foodstuffs are not important from this standpoint because of the ease in securing carbohydrate. Adequate supplies of the essentials are, however, at times difficult to secure, and it behooves the physician to instruct his patients concerning them, and to advise them to make every effort to obtain the essential nutrients by wise use of their rationing points. Every woman should be advised to include the following in her daily diet:

One quart of whole milk.

Two medium-sized oranges, three or four medium-sized apricots, four or five medium-sized stewed prunes or 8 ounces of tomato juice.

One egg.

Two to three servings of whole-grain or enriched bread or of cereal.

Two tablespoonfuls of butter or fortified margarine.

One serving of meat, fish, poultry or cheese, with liver or other organ meat once a week.

One or more cupfuls of fresh vegetables, including one green or yellow vegetable in addition to potato.

It is an accepted fact that foods vary in their nutritive values with storage, handling, cooking and preserving. From the standpoint of nutrition, liver is the richest of all meats in combined nutritive values. One serving of it contains more vitamin A and riboflavin than does a serving of any other natural food. It is an excellent source of iron, protein and thiamine, and even when cooked provides a fair amount of vitamin C. Vitamin B is water soluble and is readily destroyed by heat and by the addition of alkali to the cooking water. Since green vegetables and potatoes are good sources of thiamine before cooking, correct cooking practices should be used to preserve the vitamin in the cooked product. Since thiamine cannot be stored in the body, it is daily necessary to eat foods containing adequate amounts of it. Refinement is the enemy of thiamine, which is found in all living tissue; whole-wheat cereals, beans, pork, beef, liver and chicken are perhaps the richest sources. If care is taken to use whole-grain products, enriched and restored cereals, beans, peas and meats and to see that food is not overcooked, a deficiency of thiamine will not occur. Vitamin C is readily destroyed by heat; thus it is best taken in the form of raw vegetables and fruits. This vitamin, like vitamin B, is not stored in the body, is water soluble, and is readily destroyed by an alkali medium. Owing to the presence of 7-dehydrocholesterol, a fatlike substance,[19] in the body and to the effect of the ultraviolet rays of the sun, the aforementioned chemical substance is changed to vitamin D. Vitamin D is one of the vitamins that can be stored in the body, and when daily exposure to the sun and dietary intake causes the formation of more than is needed, the excess is naturally stored. With the presence of ultraviolet rays, either natural or artificial, the manufacturing and storage process is continuous. Thus, daily periods of sunning will help to attain adequate amounts of this vitamin, but the pregnant woman should supplement her vitamin D intake with one of the fish-liver oils. This may be taken in concentrated form with dicalcium phosphate, thus ensuring adequacy of the calcium intake as well as of that of vitamin D. Iron should be included in the diet in proprietary form as indicated, the actual amounts being determined by blood studies at the time of the first visit and during the last trimester.

Summary

The daily dietary requirements of the average pregnant woman are reviewed, and a basic list is presented of food elements that with minimal supplemental additions will provide for an adequate normal nutritive relation between the pregnant woman and the fetus.

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References

1. Williams, P. F., and Fralin, F. G. Nutrition study in pregnancy: dietary analyses of seven-day food intake records of 314 pregnant women, comparison of actual food intakes with variously stated requirements, and relationship of food intake to various obstetric factors. *Am. J. Obst. & Gynec.* 43:1-20, 1942.
2. McCance, R. A., Widdowson, E. M., and Verdon-Roe, C. M. Study of English diet by individual method: pregnant women at different economic levels. *J. Hyg.* 38:596-622, 1938.
3. Jones, O. H. Polyneuritis of pregnancy. *Am. J. Obst. & Gynec.* 45: 869-874, 1943.
4. Technical Committee, Health Commission of the League of Nations. *Problem of Nutrition.* Report on Physiological Bases of Nutrition. Vol. 2. 27 pp. London, 1936.
5. National Research Council. Committee on Food and Nutrition. *Recommended Dietary Allowances.* Washington: Government Printing Office, 1941. Pp. 1-6.
6. Waters, E. G. Weight studies in pregnancy. *Am. J. Obst. & Gynec.* 43:826-832, 1942.
7. Adair, F. L. Interrelationship of mother and fetus. *J. A. M. A.* 99: 433-437, 1932.
8. Maxwell, J. P., Hu, C. H., and Turnbull, H. M. Foetal rickets. *J. Path. & Bact.* 35:419-440, 1932.
9. Rector, J. M. Prenatal influence in rickets: fetal rickets. *J. Pediat.* 6:161-166, 1935.
10. Sontag, L. W. Significance of fetal environmental differences. *Am. J. Obst. & Gynec.* 42:996-1003, 1941.
11. Ebbs, J. H., Scott, W. A., Tisdall, F. F., Moyle, W. J., and Bell, M. Nutrition in pregnancy. *Canad. M. A. J.* 46:1-8, 1942.
12. Becker, J. E., Blickenstaff, H. J., and Eastman, N. J. Nutrition in relation to pregnancy and lactation. *Am. J. Pub. Health* 31:1265-1270, 1941.
13. Williams, P. F. Nutrition in pregnancy. *Am. J. Surg.* 48:118-124, 1940
14. Hart, B. F., and Noble, V. Calcium and quinine in labor and postpartum hemorrhage. *Am. J. Obst. & Gynec.* 45:692-696, 1943.
15. Hunscher, H. Dietary factors in pregnancy. Proceedings of the First American Conference on Obstetrics and Gynecology, Cleveland, Ohio, September, 1939.
16. Wadlow, E. E. Salt-poor diet and its effect on labor. *Am. J. Obst. & Gynec.* 39:749-756, 1940.
17. Pomerance, W., and Daichman, I. Effect of salt poor diet during pregnancy upon duration of labor. *Am. J. Obst. & Gynec.* 40:463-466, 1940.
18. Ley, L. Ueber die Behandlung des habituellen Abortus mit Vitamin C. *Munchen. Med. Wchnschr.* 84:1814-1816, 1937.
19. *The Master Menu.* Vol. I. Washington, D. C.: Office of the Quartermaster General, 1943.

CLINICAL NOTE

RUPTURE OF A LEFT TEMPORO-SPHENOIDAL BRAIN ABSCESS INTO THE VENTRICLE

Report of a Case, with Recovery

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RUPTURE of a temporosphenoidal abscess of the brain into the lateral ventricle is an event that has rightly been considered fatal. The recording of such an occurrence by roentgenograms during life, together with complete recovery following the use of one of the sulfonamide drugs, warrants the report of the present case, especially since no similar case report has been found in the literature. With increasing use of the sulfonamide drugs it is reasonable to expect recoveries in similar cases.

Report of Case

M. K., a 56-year-old, totally blind piano tuner, was first seen on January 8, 1943. He had been blind and had had a chronic mastoiditis on the left ever since the age of 5, following an attack of scarlet fever. Ten days before consultation he developed an upper acute respiratory infection that was followed by an exacerbation of the mastoiditis. Two days before, a left-facial paralysis developed. The patient had been given 4 gm. of sulfadiazine daily for the last 3 days.

Examination showed a pulsating discharge of the left middle ear with complete left-facial paralysis. The nose, throat and right eardrum were essentially normal. There was no tenderness in the mastoid areas. The neck was somewhat rigid, and a definitely positive Kernig test was obtained. There was no sensory aphasia.

The patient was referred to the Beth Israel Hospital, where x-ray films showed a sclerosed left mastoid process with no evidence of bone destruction. A lumbar puncture showed clear fluid, with a pressure of 250 mm. of water; a cell count showed 42 fresh and 3 crenated red cells and 89 white cells, with 26 polymorphonuclear leukocytes, and 63 lymphocytes. The usual postauricular radical mastoid operation was performed on January 11. A thick cortex was found, and the antrum contained foul granulating tissue under apparent pressure. Some cells along the facial canal were broken down and filled with granulating tissue and pus. There was a small area of erosion in the area of the tegmen antri 1 cm. in diameter, which was removed. The dura in this area appeared normal except for slight thickening. Cultures of material from the mastoid area showed *Staphylococcus albus* and a nonhemolytic streptococcus. The postoperative course was normal, and there was motion of the left angle of the mouth 2 days later. Sulfadiazine was given in a dosage of 6 gm. daily, the blood level being maintained at about 7 mg. per 100 cc.

On January 15, 5 days postoperatively, there was a slight rise in the temperature and the patient appeared to be somewhat drowsy. There was a definite loss of motion in the right arm and leg. The patient was sent to the operating room and a lumbar puncture was done. This showed a pressure of 250 mm. of water; the white-cell count of the fluid was 110, with 30 polymorphonuclear leukocytes and 80 lymphocytes, and the red-cell count 74. The mastoid was reopened and the area of the tegmen antri was widely exposed, leaving an area 2.5 cm. in diameter exposing the dura in this area. The dura felt tense, and granulating tissue was present. It was incised, the brain was incised, and a cannula was inserted for a distance of 3 cm., when foul-smelling, thick, creamy pus was obtained. A semirigid rubber catheter was inserted until it seemed that the bottom of the abscess was reached. The outer part of the catheter was split and sutured to the scalp in this area. Cultures of the pus showed *Staph. aureus*, diphtheroids and a nonhemolytic streptococcus. Half an hour after the patient was brought back to his room, the stupor had disappeared and most of the paralysis of the right arm and leg had cleared. Recovery was uneventful except

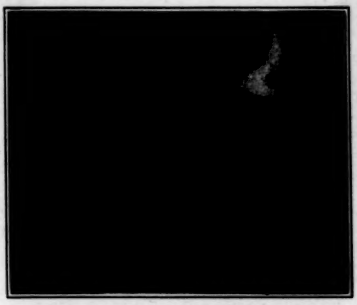

Figure 1. *Roentgenogram Showing Lipiodol in the Sinus Tract and Left Ventricle.*

for a sharp rise in temperature on January 28, at which time the temperature rose to 104°F. The dressings and catheter were changed and the sulfadiazine level, which had been maintained between 9 and 10 mg. per 100 cc., was increased by the use of sodium sulfadiazine intravenously. On the following day the sulfadiazine level was 13.9 mg. The temperature returned to normal, and the postoperative course was uneventful except for the discharge, which had become watery with a small amount of visible pus.

Figure 2. *Roentgenogram, Taken with the Patient Face Down and Showing Lipiodol in the Sinus Tract and Both Anterior Horns, and Air and Droplets of Lipiodol Scattered Through the Left Ventricle.*

One week later, it was decided to ascertain the size of the cavity. At the suggestion of the roentgenologist, lipiodol (about 5 cc.) was inserted in the cavity through the catheter until there was an overflow. X-ray films were taken immediately, the report being as follows:

A sinus tract was visualized extending first in the direction of the tube. It was 0.5 cm. in width and irregular in contour. The oil had entered the inferior horn of the left ventricle from its lowermost medial aspect and it was first seen filling this lower horn (Fig. 1). After some time it

shifted throughout the ventricular system and there was only a faint coating in the left lower horn. Stereo x-rays taken in the anteroposterior and left lateral positions revealed additional facts as follows: In the face-down position, a larger amount of the oil occupied the left anterior horn. A group of droplets was seen in the right anterior horn (Fig. 2). The left posterior horn was filled with

FIGURE 3. *Roentgenogram Showing Lipiodol in the Anterior Horn, Posterior Horn and Sinus Tract, and Air and Lipiodol in the Temporal Horn.*

air, and there were several small lipiodol droplets and small air-filled spaces that could not be identified. The lateral view taken in the left position showed about the same distribution of oil (Fig. 3). There was air filling of the dilated right lower horn.

Recovery was uneventful. Further x-ray films showed lipiodol at the base of the spinal column. The catheter was gradually shortened and the sulfadiazine gradually diminished. The catheter was finally removed, and the patient was discharged on February 8. X-ray films taken on March 19 showed small droplets of lipiodol in both the lower and posterior horns and along the basal cisternas. There was no evidence of intracranial air.

In May the patient returned to his work and has continued well to the present writing.

COMMENT

Abscess of the brain secondary to a chronic mastoiditis is always a grave event. Many cases go undiagnosed and terminate fatally before appropriate therapy can be given. In the present case, although the diagnosis was evident and surgery had been performed, development of sudden hemiplegia led to the diagnosis of the extension of the abscess into the brain tissue. The abscess was drained, following which lipiodol injected into the cavity showed connection of the abscess with the ventricle. It appears that the use of a high concentration of sulfadiazine probably checked further spread of the infection.

Rupture of such an abscess into the ventricle is extremely rare, and is generally seen only at autopsy. X-ray studies of such an event in life have not heretofore been made.

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MEDICAL PROGRESS

BLOOD BANKS AND BLOOD TRANSFUSION*

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BLOOD transfusion and the use of various blood derivatives are among the most useful and commonest forms of therapy. The recent great increase in the use of transfusion therapy has been due largely to the increasing recognition of the benefits to be derived from administration of blood or plasma in a wide variety of diseases, to the practical development of blood banks, which have made the administration of blood and plasma extremely simple and economical, and to the need of the military services for plasma and blood. Each of the numerous preparations of blood and plasma now available — unmodified blood, fresh citrated blood, blood stored in various mixtures of citrate and glucose, suspensions of erythrocytes, refrigerated plasma, frozen plasma, desiccated plasma and various preparations of purified albumin and globulin — has certain advantages and certain limitations that make it especially useful in some conditions but unsatisfactory in others. Transfusion of blood or plasma is often of value in the following diseases: anemia; hemorrhagic diseases; hemorrhage, shock and burns; hypoproteinemia and infections. The preparations most satisfactory in the treatment of each of these conditions will be discussed, as well as the necessary precautions and the commoner transfusion reactions.

Several excellent books dealing with blood transfusion and blood banks have appeared during the last few years. Kilduffe and DeBakey[1] have thoroughly reviewed the entire literature of transfusion and present excellent practical information on the establishment and operation of a blood bank. Wiener[2] has again revised his classic monograph, *Blood Groups and Transfusion*, and has added valuable chapters on the Rh factor and on the use of stored blood. Mudd and Thalhimer[3] have edited a collection of papers on the theoretical and practical

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aspects of blood and blood-substitute therapy that summarizes most of the important American contributions on these topics. Riddell[4] discusses the practical details of transfusion therapy.

Anemia

The use of transfusion in the treatment of anemia is directed toward increasing the oxygen-carrying capacity of the blood and is achieved by supplying physiologically functional erythrocytes to the recipient. In certain cases of acute hemolytic anemia, in patients who have sustained a large and rapid loss of blood from hemorrhage, and in some acute types of bone-marrow depression transfusion is often a life-saving, emergency procedure. In certain chronic hemolytic anemias, and in patients with chronic bone-marrow depression (aplastic anemia, myelophthisic anemia, uremia and hepatic disease), transfusions may sustain life for months and occasionally years. Fortunately, the anemias most frequently encountered — iron-deficiency anemia and pernicious anemia — usually respond rapidly to iron or liver-extract therapy, and transfusion in such cases is rarely necessary, even when the red-cell count falls to levels as low as 1,000,000.[5] Preoperative and postoperative transfusions are of considerable value in anemic patients who must undergo immediate surgery and in those in whom considerable blood loss may occur. Such transfusions aid in the prevention of shock and shorten the convalescent period.

To be successful, the transfusion treatment of anemia must provide the recipient with functional erythrocytes that will survive during the acute phase of the disease. There is little doubt that erythrocytes transfused immediately after withdrawal from a donor fulfill this requirement. Several investigators[6–8] have demonstrated the survival of transfused erythrocytes for periods of one hundred and twenty to one hundred and thirty days, and the clinical efficacy of transfusions of fresh blood is practical proof that such cells survive during the critical periods of anemia.

Considerable controversy has arisen concerning the relative merits of unmodified blood and citrated blood for transfusion purposes.[9, 10] Although the administration of unmodified blood is more physiologic than that of citrated blood and in skillful hands apparently produces slightly fewer reactions, it requires an exacting technic and always carries the danger of introducing blood clots or air emboli into the veins of the recipient. From a practical standpoint, the use of citrated blood is much more convenient, safer and just as satisfactory therapeutically.[11] Sodium citrate is relatively nontoxic, since 6 to 8 gm. may be injected intravenously during a ten-minute period without producing symptoms,[12] and larger quantities may be given over longer periods of time without ill effect. It is rapidly oxidized and excreted, 90 per cent being removed from the blood within ten minutes.[13] Transfusions of even large amounts of citrated blood are not likely to produce symptoms of citrate toxicity, since the citrate contained in 2500 cc. of citrated blood (6.25 gm.) is less than the toxic dose, and furthermore, a considerable amount of the citrate is metabolized during the time required to administer this volume of blood.

Sodium citrate exerts little or no effect on the post-transfusion survival of erythrocytes provided citrated blood is administered to the recipient within a few hours of the time it is withdrawn from the donor.[6–8, 14] Longer storage, however, exerts an extremely deleterious effect on erythrocytes, the post-transfusion survival of such cells varying inversely with the length of time that the blood is stored.[7, 8, 14, 15] Eighty per cent of the erythrocytes of citrated blood stored for seven days or longer are destroyed within twenty-four hours after transfusion,[8, 14] and consequently such blood is quite unsatisfactory for use in the treatment of anemia. Furthermore, transfusions of blood stored for too long a time may actually be dangerous because the hemolysis of the transfused cells is sometimes so rapid that hemoglobinemia and hemoglobinuria occur.[16, 17]

Rous and Turner[18] observed that the addition of glucose to citrated blood decreased its tendency to undergo spontaneous hemolysis and presumably prolonged the survival of stored cells in vivo after transfusion. The large volume (1666 cc.) of this mixture and the amount of sodium citrate (12.6 gm.) required for the preservation of 500 cc. of blood make impractical the use of this preservative, although it preserves erythrocytes fairly well.[18, 19, 20] During the last ten years, under the stimulus of war and the rapidly developing civilian blood-bank services, an intensive search for better erythrocyte preservatives has been carried on in most civilized countries. The greatest stumbling block encountered in these studies has been the difficulty of assessing the value of any given preservative. Numerous in vitro studies of blood preservatives have been made,[21–27] but these appear to have little positive value in indicating the probable behavior of erythrocytes after transfusion. It has now been established fairly definitely that the prevention of in vitro hemolysis, the preservation of relatively normal fragility to hypotonic saline solutions, various lytic agents and trauma, the maintenance of relatively normal potassium and phosphate concentrations within the cells and a normal pH have little significance in indicating the length of survival of stored cells after they are transfused.[7, 15, 20, 28] Unfortunately, most investigators of cell preservatives have employed one or more of these criteria in evaluating the efficacy of their preparations, and have failed to put them to the only test that is of actual significance — that is, the survival in vivo of the stored erythrocytes after transfusion.

Attempts to determine on a quantitative basis the actual length of survival of transfused cells have been made with differential agglutinating technics[6-8, 15, 29] and with the use of radioactively labeled erythrocytes.[16, 17, 30] Although both methods are subject to criticism, it is apparent from such studies that cells can be stored in glucose-citrate mixtures for at least two weeks, with an expected survival of 80 to 90 per cent of the transfused cells for at least forty-eight hours after transfusion. A glucose-citrate mixture buffered with sodium phosphate to a pH of 7.4 has been recommended by Denstedt and his associates[29] and appears to be one of the most satisfactory preservatives studied.

Although this preservative is satisfactory for use in civilian blood banks, it has not as yet been developed sufficiently to allow shipment of whole blood to the battlefronts. Consequently, to supply the military services with a blood substitute plasma must still be separated from blood and the erythrocytes discarded. Attempts are being made to salvage these discarded erythrocytes and to make them available for transfusion purposes. They have been resuspended in various saline and glucose solutions and administered to patients in the same way that whole-blood transfusions are given.[31, 32] Therapeutic response to such erythrocyte suspensions has apparently been about the same as would have been achieved from administering erythrocytes preserved in citrated blood for the same length of time. Such suspensions do not prolong the allowable preservation period of erythrocytes, but they do allow the use of waste red cells from plasma-processing centers. Erythrocytes stored in blood banks are as a rule unsatisfactory for transfusion purposes by the time the plasma is separated from them, and resuspension of such old cells in the fluids so far studied cannot be expected to restore their potentiality of post-transfusion survival.

The interesting possibility exists that the breakdown products of transfused erythrocytes accelerate the production of new red cells by the bone marrow. Cruz, Hahn and Bale[33] observed that radioactive iron liberated from erythrocytes by acetylphenylhydrazine hemolysis was rapidly reutilized for the synthesis of new hemoglobin. Ross and Chapin[14] found that although transfused red cells might be rapidly destroyed, the hemoglobin iron of these cells quickly reappeared in newly formed erythrocytes, and the rate of reutilization of this hemoglobin iron was much more rapid than it would have been if iron alone had been given by injection. These observations suggest that even though donor erythrocytes are broken down a few days after transfusion, they may furnish easily utilizable building stones for the formation of new red cells.

Solutions of hemoglobin have been advocated as a substitute for blood,[34] and Amberson and his associates,[35, 36] have been able to maintain life in cats with such solutions. The hazards associated with the administration of the required amounts are too great to justify their clinical use, and in spite of their capacity to combine with and liberate oxygen[37] it is unlikely that they can ever be expected to replace or even supplement the physiologic activity of erythrocytes.

In summary, if it is desired to supply functional erythrocytes to a recipient, fresh citrated blood is probably the most desirable preparation to use, but citrated blood stored not longer than two days can be used, and blood stored in glucose-citrate mixtures for one or two weeks may also be satisfactory.

Hemorrhagic Diseases

Transfusion is the only effective treatment for several types of hemorrhagic disease, and is still of considerable value in the control of several other types for which more specific therapeutic measures are now available. It is used in these diseases to supply some substance that is essential for the proper functioning of the clotting or hemostatic mechanisms but that is decreased in amount or absent in the diseased patient. The classic theory of blood coagulation is still of considerable aid in considering the hemorrhagic diseases from a therapeutic viewpoint, although it is undoubtedly oversimplified and should not be accepted too literally.

Prothrombin (in plasma) + Thromboplastin (in platelets, tissues and possibly plasma) + Calcium (in plasma) → Thrombin (in plasma)

Fibrinogen (in plasma) + Thrombin → Fibrin (clots)

Interference with any one of these factors delays or prevents the clotting of blood, but from the practical clinical standpoint disturbances of only two of these factors — prothrombin and thromboplastin — are encountered.

Prothrombin deficiency is now known to be the cause of hemorrhagic disease of the newborn, and of the hemorrhagic states encountered in cases of biliary obstruction and of severe liver damage and in diseases of faulty absorption of fat and the fat-soluble vitamins — for example, sprue and ulcerative colitis. The anticoagulant drug dicoumarin produces its effect by depressing the formation of prothrombin. Parenteral administration of vitamin K controls many of these conditions, but it does not elevate the plasma prothrombin or control a hemorrhagic tendency if liver damage is severe.[38] Furthermore, the latent period before the effect of vitamin K can become manifest and decrease the bleeding tendency is occasionally too long, even in patients with normal hepatic function. In such cases transfusion of blood or plasma is the only effective means of increasing plasma prothrombin, and if administered in adequate amounts these substances will control even the severest cases of prothrombin deficiency.[39]

It is important to remember, however, that prothrombin is a labile substance and is rapidly destroyed in alkaline solutions[40] and in blood or plasma kept at room temperatures. Prothrombin activity is lost more slowly at 4°C.,[41-43] and plasma separated from freshly drawn blood and frozen immediately maintains most of its prothrombin activity for several months.[44] Prothrombin is also preserved in desiccated blood plasma, but is destroyed during reconstitution if the reaction of the solution is not maintained near neutrality.[40] Reconstitution of desiccated blood plasma with a 0.1 per cent solution of citric acid instead of with distilled water keeps the reaction of the plasma near neutrality and maintains a satisfactory prothrombin content.

The greatly prolonged clotting time encountered in hemophilia is now known to be due to a deficiency of thromboplastin. It was formerly believed that this deficiency was due to abnormal resistance of the blood platelets, which were supposed not to break down and liberate thromboplastin in the normal fashion.[45] It now appears that a more important deficit exists in the plasma itself. Patek and Stetson[46] and Lozner, Kark and Taylor[47] demonstrated the efficacy of platelet-free normal human plasma in reducing the coagulation time of hemophilic blood, both in vitro and in vivo, and showed that plasma from hemophilic subjects contains decreased amounts of this active thromboplastin-like substance. Subsequent investigations by Taylor and his associates,[48-50] have shown that normal plasma contains a so-called "globulin substance" effective in accelerating blood coagulation in cases of hemophilia. This substance is apparently quite stable and is well preserved in blood or plasma kept at 4°C. and in frozen and desiccated plasma. Injections of any of these preparations usually serve to prevent or control the hemorrhages of hemophilic patients. Purified preparations of globulin substance[51] and of rabbit thrombin[52] have also been prepared that have been efficacious as local hemostatic agents in normal as well as in hemophilic subjects.

Except for splenectomy, transfusion of fresh blood is the only procedure of specific therapeutic value in patients with thrombocytopenic purpura, and occasionally even fresh blood fails to reduce the bleeding time or to allay hemorrhage in this disease. The characteristic marked reduction of platelets does not interfere with the clotting mechanism itself, but is responsible for the failure of the clot to retract, and perhaps for the prolonged bleeding time. The exact relation between the capillary abnormality existent in this disease[53] and the decrease in blood platelets is obscure, but as a rule transfusion of fresh blood does increase the platelets of the recipient and decrease the bleeding time.[54] There is little difference in this respect between the efficacy of unmodified blood and that of fresh citrated blood, but injections of stored bank blood or plasma have been shown to have little effect in controlling the hemorrhagic tendency, probably because of the rapid degeneration of the blood platelets in stored blood.[55]

Hemorrhage

The plasma and erythrocytes lost during acute hemorrhage are best replaced by transfusions of blood, although plasma may be used if the loss of red cells has not been excessive. In cases of extreme blood loss in which the hemoglobin concentration has fallen to extremely low levels blood should be used, since administration of plasma will further dilute the remaining cells and precipitate or aggravate tissue anoxia.[56] In treating patients with hemorrhage it is essential to combat or prevent a reduction in the effective blood volume before actual shock occurs, and transfusion must never be delayed until the blood pressure begins to fall or signs of tissue anoxia appear, since it is far easier to prevent the onset of shock than it is to treat it once it has developed.[57]

The belief that transfusion of blood in cases of gastrointestinal bleeding may raise the blood pressure and actually "blow off" the clot from the bleeding site is erroneous. The rapid infusion of 500 cc. of blood within five or ten minutes produces an elevation of blood pressure of only 10 mm. of mercury,[58] and Kordenat[59] demonstrated experimentally that such increase of pressure is inadequate to dislodge recently formed thrombi from small arteries. Clinical experience has also proved that the transfusion of blood in cases of bleeding duodenal ulcer is frequently a life-saving measure and does not precipitate a recurrence of hemorrhage.[60]

The transfusion of unmodified blood in the treatment of hemorrhage has been advocated in the belief that it is more effective than citrated blood in promoting coagulation and hemostasis. The greater availability of citrated blood in blood banks and the rapidity and ease with which such blood can be procured and administered in cases of emergency appear to outweigh the slight advantages claimed for unmodified blood.[58] Theoretically, fresh blood may be more effective than stored blood because of the degeneration of platelets and prothrombin in the latter, but practically, stored blood is quite satisfactory.

Bleeding into the pleural or peritoneal cavity may be so excessive that shock is produced. Autotransfusion — the transfusion of this blood into the patient's veins — has been suggested as an emergency procedure.[61] The mortality from such transfusions has been between 2 and 4 per cent,[61-63] death usually being attributable directly to infusion of contaminated blood or of blood that has remained in the peritoneal cavity for seventy-two hours or longer. Because of the danger of the procedure it should be employed only in cases of extreme emergency when other blood or plasma cannot be obtained.

(*To be concluded*)

References

1. Kilduffe, R. A., and DeBakey, M. *The Blood Bank and the Technique and Therapeutics of Transfusions.* 558 pp. St. Louis: C. V. Mosby Company, 1942.
2. Wiener, A. S. *Blood Groups and Transfusion.* 438 pp. Third edition. Springfield: Charles C Thomas, 1943.
3. Mudd, S., and Thalhimer, W. *Blood Substitutes and Blood Transfusion.* 407 pp. Springfield: Charles C Thomas, 1942.
4. Riddell, W. H. *Blood Transfusion.* 370 pp. New York & London: Oxford University Press, 1939.
5. Wintrobe, M. M. *Clinical Hematology.* 792 pp. Philadelphia: Lea and Febiger, 1942. P. 264.
6. Wiener, A. S., and Schaefer, G. Limitations in use of preserved blood for transfusion: study of fate of transfused erythrocytes in recipient's circulation. *M. Clin. North America* **24**:705-722, 1940.
7. Mollison, P. L., and Young, I. M. On survival of transfused erythrocytes of stored blood. *Quart. J. Exper. Physiol.* **30**: 313-327, 1941.
8. Belk, W. P., and Barnes, B. C. Survival time after transfusion of erythrocytes of citrated human blood stored at 4 to 6° centigrade. *Am. J. M. Sc.* **201**:838-841, 1941.
9. Beck, R. C. Sodium citrate and unmodified blood transfusions: relative merits, frequency, and cause of reactions. *South. Med. & Surg.*, **96**:255-266, 1934.
10. Kilduffe and DeBakey.[1] Pp. 375-377.
11. Wiener.[2] P. 94.
12. Neubof, H., and Hirshfeld, S. Slow intravenous administration of large doses of sodium citrate: new method for control of bleeding. *New York M. J.* **113**:95-98, 1921.
13. Salant, W., and Wise, L. E. Action of sodium citrate and its decomposition in body. *J. Biol. Chem.* **26**:27-58, 1916-17.
14. Ross, J. F., and Chapin, M. A. Effect of storage of citrated blood on survival of transfused erythrocytes. *J. A. M. A.* **123**:827-829, 1943.
15. Mollison, P. L., and Young, I. M. In vivo survival in human subject of transfused erythrocytes after storage in various preservative solutions. *Quart. J. Exper. Physiol.* **31**:359-392, 1942.
16. Strumia, M. M. Symposium on new trends in surgery: fate of transfused refrigerated blood and problem of blood banks. *S. Clin. North America* **22**:1693-1715, 1942.
17. Ross, J. F. Unpublished data.
18. Ross, F., and Turner, J. R. Preservation of living red blood cells in vitro: methods of preservation. *J. Exper. Med.* **23**:219-237, 1916.
19. Robertson, O. H. Transfusion with preserved red blood cells. *Brit. M. J.* **1**:691-695, 1918.
20. Maizels, M. Phosphate, base and haemolysis in stored blood. *Quart. J. Exper. Physiol.* **33**:143-181, 1943.
21. Belk, W. P., Henry, J. W., and Rosenstein, F. Observations on human blood stored at 4 to 6° centigrade. *Am. J. M. Sc.* **198**: 631-633, 1939.
22. Belk, W. P., and Rosenstein, F. Effect of glucose in preservation of citrated human blood stored at 4° to 6° centigrade. *Am. J. M. Sc.* **201**:841-847, 1941.
23. DeGowin, E. L., Harris, J. E., and Plass, E. D. Studies on preserved human blood: various factors influencing hemolysis. *J. A. M. A.* **114**:850-855, 1940.
24. *Idem.* Studies on preserved human blood. II. Diffusion of potassium from erythrocytes during storage. *J. A. M. A.* **114**:855-857, 1940.
25. DeGowin, E. L., Hardin, R. C., and Harris, J. E. Studies on preserved human blood. III. Toxicity of blood with high plasma potassium transfused into human beings. *J. A. M. A.* **114**:858, 1940.
26. DeGowin, E. L. Storage, transportation and administration of whole blood. In Mudd and Thalhimer.[3] Pp. 277-296.
27. Maizels, M., and Whitaker, N. Effects of storage on human erythrocytes. *Lancet* **1**:113-116, 1940.
28. Mollison, P. L., and Young, I. M. Failure of in vitro tests as guide to value of stored blood. *Brit. M. J.* **2**:797-800, 1941.
29. Denstedt, O. F., Osborne, D. E., Stansfield, H., and Rochlin, I. Survival of preserved erythrocytes after transfusion. *Canad. M. A. J.* **48**:477-486, 1943
30. Hahn, P. F., Balz, W. F., and Balfour, W. M. Radioactive iron used to study red blood cells over long periods: constancy of total blood volume in dog. *Am. J Physiol.* **135**:600-605, 1942.
31. Evans, R. S. Use of concentrated red cells as substitute for whole blood in transfusion therapy of anemia. *J. A. M. A.* **122**:793-796, 1943.
32. Murray, C. K., Hale, D. E., and Shaar, C. M. Preparation and use of red blood cell suspensions in treatment of anemia. *J. A. M. A.* **122**:1065-1067, 1943.
33. Cruz, W. O., Hahn, P. F., and Bale, W. F. Hemoglobin radioactive iron liberated by erythrocyte destruction (acetylphenylhydrazine) promptly reutilized to form new hemoglobin. *Am. J. Physiol.* **135**: 595-599, 1942.
34. O'Shaughnessy, L., Mansell, H. E., and Slome, D. Haemoglobin solution as blood substitute. *Lancet* **2**:1068, 1939.
35. Amberson, W. R., Jacobs, J., Hisey, A., and Monks, J. V. Hemoglobin-saline solutions as transfusion media. In Mudd and Thalhimer.[4] Pp. 156-169.
36. Amberson, W. R., Flexner, J., Steggerda, F. R., Mulder, A. G., Tendler, M. J., Pankratz, D. S., and Lang, E. P. On use of Ringer-Locke solutions containing hemoglobin as substitute for normal blood in mammals. *J. Cell. & Comp. Physiol.* **5**:359-382, 1934.
37. Hartridge, H., and Roughton, F. J. W. Rate of distribution of dissolved gases between red blood corpuscle and its fluid environment: preliminary experiments on rate of uptake of oxygen and carbon monoxide by sheep's corpuscles. *J. Physiol.* **62**:232-242, 1927.
38. Bollman, J. L., Butt, H. R., and Snell, A. M. Influence of liver on utilization of vitamin K. *J. A. M. A.* **115**:1087-1091, 1940.
39. Clute, H. M. Hemorrhage in obstructive jaundice: case report with recovery after twelve transfusions. *S. Clin. North America* **13**: 609-615, 1933.
40. Strumia, M. M. Preservation of prothrombin in dried plasma. *J. A. M. A.* **119**:710, 1942.
41. Rhoads, J. E., and Panzer, L. M. Prothrombin time of "bank blood." *J. A. M. A.* **112**:309, 1939.
42. Warner, E. D., DeGowin, E. L., and Seegers, W. H. Studies on preserved human blood: decrease in prothrombin titer during storage. *Proc. Soc. Exper. Biol. & Med.* **43**:251-254, 1940.
43. Kolmer, J. A. Studies on preservation of human blood. *Am. J. M. Sc.* **200**:311-321, 1940.
44. Strumia, M. M., and McGraw, J. J. Blood plasma: its place in practice of medicine, with special consideration to problems of preservation. *J. A. M. A.* **118**:427-429, 1942.
45. Minot, G. R., and Lee, R. I. Blood platelets in hemophilia. *Arch. Int. Med.* **18**:474-495, 1916.
46. Patek, A. J., Jr., and Stetson, R. P. Hemophilia: abnormal coagulation of blood and its relation to blood platelets. *J. Clin. Investigation* **15**:531-542, 1936.
47. Loxner, E. L., Kark, R., and Taylor, F. H. L. Coagulation defect in hemophilia: clot promoting activity in hemophilia of Berkefelded normal human plasma free from fibrinogen and prothrombin. *J. Clin. Investigation* **18**:603-608, 1939.
48. Patek, A. J., Jr., and Taylor, F. H. L. Hemophilia: some properties of substance obtained from normal human plasma effective in accelerating coagulation of hemophilic blood. *J. Clin. Investigation* **16**:113-124, 1937.
49. Pohle, F. J., and Taylor, F. H. L. Coagulation defect in hemophilia: effect in hemophilia of intramuscular administration of globulin substance derived from normal human plasma. *J. Clin. Investigation* **16**:741-747, 1937.
50. Loxner, E. L., and Taylor, F. H. L. Coagulation defect in hemophilia: studies of clot promoting activity associated with plasma euglobulin in hemophilia. *J. Clin. Investigation* **18**:821-825, 1939.
51. Pohle, F. J., and Taylor, F. H. L. Use of globulin substance derived from beef plasma as a local hemostatic in hemophilia. *J. Clin. Investigation* **17**:677-682, 1938.
52. Loxner, E. L., MacDonald, H., Finland, M., and Taylor, F. H. L. Use of rabbit thrombin as local hemostatic. *Am. J. M. Sc.* **202**: 593-598, 1941.
53. MacFarlane, R. G. Critical review: mechanism of haemostasis. *Quart. J. Med.* **10**:1-29, 1941.
54. Krasso, H. Ueber den Wert und die Wirkungsweise der Bluttransfusion bei der thrombopenischen Purpura. *Wien. Arch. f. ins. Med.* **14**:377-404, 1927.
55. Kolmer, J. A. Preserved citrated blood "banks" in relation to transfusion in treatment of disease with special reference to immunologic aspects. *Am. J. M. Sc.* **197**:642-652, 1939.
56. Black, D. A. K., and Smith, A. F. Blood and plasma transfusion in alimentary hemorrhage. *Brit. M. J.* **1**:187-192, 1941.
57. Polayes, S. H., and Morrison, M. Study on results of 1500 transfusions in 1000 cases. *Am. J. M. Sc.* **184**:326-336, 1932.
58. Wiener.[2] P. 78.
59. Kordenat, R. A. Relation of blood transfusion to disturbance of blood clot formation. *Mil. Surgeon* **66**:206-214, 1930.
60. Allen, J. G. Acute massive hemorrhage from upper gastrointestinal tract, with special reference to peptic ulcer. *Surgery* **2**:713-731, 1937.
61. Watson, C. M., and Watson, J. R. Autotransfusion: review of American literature with report of two additional cases. *Am. J. Surg.* **33**: 232-237, 1936.
62. Ricci, J. V., and DiPalma, S. Analysis of 100 cases of ruptured ectopic gestation: technic and evaluation of autohemolusion. *Am. J. Obst. & Gynec.* **22**:857-867, 1931.
63. Dörr, H., and Hoffmann, W. Erfahrungen bei der ektopischen Schwangerschaft auf Grund unserer Beobachtungen in den Jahren 1912-1938. Kritische Untersuchungen über die Reinfusion des Bauchhöhlenblutes. *Arch. f. Gynäk.* **169**:31-37, and 38-52, 1939.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 30061

PRESENTATION OF CASE

A twenty-three-year-old woman was admitted because of swelling in the lower back of three months' duration.

The patient had been in excellent health until about eight months before entry, when she developed pain in the lower midback. This was severe only when she tried to bend, and it did not radiate. It lasted for about five months, improving slowly but steadily. Three months before admission she noted the gradual onset of swelling in the lower midback. The swelling increased in size, but there was no pain. She had no weakness in the back or legs or any other symptoms.

One sister had arrested tuberculosis.

Physical examination showed a well-developed, well-nourished girl in no distress. The heart was normal. Slight "wheezes" were heard in the right lung. The abdomen was normal. A cystic, fluctuant, soft mass measuring about 15 cm. in diameter was found in the midlumbar region. No neurologic abnormalities were noted.

The blood pressure was 100 systolic, 80 diastolic. The temperature was 98.6°F., the pulse 90, and the respirations 20.

Examination of the blood showed a white-cell count of 11,300. The hemoglobin was 12.8 gm. per cent. The urine was negative. A blood Hinton test was negative, and a blood Wassermann doubtful. A lumbar puncture showed initial pressure of 120 mm. of water, with normal dynamics. Forty centimeters of clear fluid was withdrawn, which contained 3 white cells and no red cells per cubic millimeter; the total protein was 24 mg. per 100 cc., and the gold-sol curve 0000000000. A Wassermann test was negative. Pressure on the tumor gave no rise in the manometer.

Roentgenograms of the spine showed destructive changes in the dorsal portion of the spinous process of the fourth lumbar vertebra. This spinous process lay within and appeared to extend into the area of soft-tissue swelling. There was no evidence of involvement of the neural arch, aside from the spinous process. The fifth lumbar vertebra was intact. An air myelogram showed the air column poorly outlined in the lateral but clearly visible in the anteroposterior view. It was visualized only below the level of the fourth lumbar vertebra. The nerve sheaths were not filled. The cul-de-sac extended to the level of the second sacral segment and was normal in appearance. There was failure of closure of the spinal canal below the third sacral segment. No connection could be seen between the spinal canal and the mass posterior to the sacrum on the right side.

On the tenth hospital day an operation was performed.

*On leave of absence.

DIFFERENTIAL DIAGNOSIS

DR. JAMES B. AYER: We are not told at what levels the lumbar puncture and the air myelogram were done.

DR. JOST MICHELSEN: They were both done at the same time. The needle was put in the interspace between the second and the third lumbar vertebra.

DR. AYER: Apparently there were two destructive areas, one in the lower sacral region and one in the spinous process of the fourth lumbar vertebra. Perhaps we should see the x-ray films.

DR. LAURENCE L. ROBBINS: These films were taken at the time of the air myelogram but with a different technic from that which would best demonstrate the soft-tissue mass. I think we can make it out in this area. It apparently extends from about the posterior margin of the spinous process of the second lumbar down to approximately the second sacral segment. There is definite destruction of the spinous process of the fourth lumbar vertebra, which is apparently at about the center of the mass. I do not believe that this is a congenital anomaly, but rather a destructive process. So far as the air myelogram is concerned, it is not a satisfactory examination. I do not see any evidence of an inflammatory process encroaching on the spinal canal. There is evidence of congenital anomalies. The sacral hiatus is larger than usual, and there is incomplete fusion of the laminas of the first sacral segment, as well as an anomaly in the development of the articular facets of the third lumbar vertebra; but these things are of no practical importance.

DR. AYER: In the transcription it says that the air column stopped below the fourth lumbar vertebra. Is that your interpretation?

DR. ROBBINS: As I said before, the air myelogram was unsatisfactory; but I think that there was air all through the lumbar canal. The only way one could be sure would be to stereoscope these films in the anteroposterior view.

DR. AYER: Then the dogmatic statement "It was visualized only below the level of the fourth lumbar vertebra" is not borne out.

DR. ROBBINS: That is someone's opinion who had the opportunity to stereoscope the films. I should think there was air going up to the first lumbar vertebra.

DR. AYER: A good deal depends on this point, and I should like to say that the experience of some of us with air myelograms has not been entirely satisfactory. I prefer lipiodol. On the other hand, the members of a good many other clinics believe that they can outline a disk, which is something smaller than what we have here. So there is a difference of opinion in the interpretation of air myelograms.

We are told that the physical and neurologic examinations were negative, except for a lump the size of a grapefruit in the midlumbar region. Therefore discussion must center primarily on this mass. It was said to be cystic and fluctuant, and there was no pain connected with it, except when she bent her back. It enlarged rapidly, although we need not assume that its growth was limited to three months — perhaps eight months is a more reasonable estimate. As no note is made we may perhaps assume that the mass was neither tender, discolored nor warm to touch. Nor are we told whether it was attached to the skin or deep structures.

From the evidence, I think we can safely say that we are concerned with a rapidly growing mass situated slightly to the right of the midline in the low lumbar region, which contained fluid but was noninflammatory, and was not accompanied by gross destruction of the vertebras. Therefore, we can eliminate both pyogenic and tuberculous abscess, and also cancer originating in a vertebra. Tumors such as sarcoma and neurofibroma are firm and resilient, not primarily cystic, and may also be eliminated. By far the commonest fluctuant mass in this region is the meningocele, and the description given suggests this, although I miss the presence of the characteristic dimpling of skin and lanugo hair so characteristically seen. Nor is it likely that a meningocele, and even more likely a meningomyelocele, would be present with no disturbance of nerve function, particularly weakness and deformity of feet and bladder incontinence. Nor was there the characteristic lumbar defect in the spine. Nor was there fluid in this mass that connected with the subarachnoid space. I am forced to consider the embryonal tumors that occur in this region. Chordoma, which I believe is always firm and gives a characteristic x-ray picture of wide, clear-cut destruction of the sacrum, seems unlikely. But dermoid cyst and perhaps lipoma seem to answer the characteristics given. Both are associated with imperfections in the spine.

Was the spinal canal invaded? From the original interpretation of the air myelogram we are led to believe a block existed at the level of the fourth lumbar vertebra, but review of the films by Dr. Robbins fails to confirm this interpretation. Certainly there was no clinical evidence of involvement of the cauda equina, and yet we have often seen the lumbosacral canal filled with tumor — especially lipoma — without clinical evidence of its presence.

I therefore believe that the diagnosis that best fits this condition is a dermoid cyst, probably but not necessarily with attachment to the meninges through the imperfect spine; lipoma is my second choice.

DR. MAURICE FREMONT-SMITH: May I ask whether cold abscess starting in the spine might not make this picture? You mentioned it, but you then hastily discarded it.

DR. AYER: I threw it out rapidly and did not give all the reasons. I think it is fair to assume that the mass had been there for eight months and, if tuberculous, should have shown more spinal destruction than it did. Does not Pott's disease start from the body rather than from the spinous process? Nor do I remember seeing it in the lumbosacral region. There was no fever. A sister had tuberculosis, but not the patient. Perhaps I threw out tuberculosis too nonchalantly but I do not believe that it is likely.

DR. ROBBINS: Is destruction of the spinous process frequent in lipoma or dermoid?

DR. AYER: Not in lipoma. In dermoid cysts, however, I believe that there are rests in the spinous processes as well as in the lateral masses. That is a point in embryology of which I am not sure.

DR. ROBBINS: Yes, I think there can be; but the thing that is impressive here is that it appears to have been a destructive process and not an erosive one.

DR. AYER: That is the weak point in the argument.

DR. ROBBINS: I should expect to see erosion of the spinous process.

DR. AYER: I rather wanted to have it a developmental defect. Perhaps it is unreasonable to say that I still wonder if it could have been originally a developmental defect because of the other anomalies that you have demonstrated. If I could have that leeway it satisfies me. Certainly an osteomyelitis starting there would not give this picture.

DR. ROBBINS: It could give that appearance in the spinous process.

DR. AYER: Yes, but hardly the rest of the picture, with the normal temperature and so forth.

DR. BENJAMIN CASTLEMAN: Dr. Kubik saw this patient before operation.

DR. CHARLES S. KUBIK: I do not remember the case well except that I missed the diagnosis. Perhaps Dr. Michelsen remembers it.

DR. MICHELSEN: Several points were not brought out in the summary that perhaps would have been of some value to Dr. Ayer. First of all, the size of the tumor increased on straining, sneezing and coughing, which made it fairly evident that the tumor contained fluid; but it did not transilluminate. There was also some tenderness to palpation.

It was decided to do an air myelogram not so much because we were hunting for an obstruction or a tumor in the spinal canal, but because we wanted to find out whether the mass was connected with the subarachnoid space. When this decision was made the destruction of the spinous process of the fourth lumbar vertebra had not been reported. The first x-ray films were read as negative.

On biopsy of the tumor a large amount of greenish pus was obtained and a small piece of bone was found at the bottom of the abscess.

CLINICAL DIAGNOSIS (preoperative)

Tumor of lower back (? hemangioma).

DR. AYER'S DIAGNOSIS

Dermoid cyst?
Lipoma?

ANATOMICAL DIAGNOSIS

Tuberculosis of spinous process of fourth lumbar vertebra.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The material we received showed caseous tuberculosis.

DR. MICHELSEN: After the diagnosis of a cold abscess was established, Dr. George W. Van Gorder was called in consultation. He stated that he had seen a similar lesion in that location, but that the condition was extremely rare. A detailed clinical checkup revealed that the patient had incipient tuberculosis of the lungs, and she was discharged to a tuberculosis sanatorium.

DR. AYER: The "wheezes" meant something after all.

CASE 30062

PRESENTATION OF CASE

A sixty-three-year-old tool inspector entered the hospital because of severe pain in the anterior chest of four months' duration.

The patient was in good health until about ten months before entry, when he developed a severe, dry cough and "bronchitis," which caused nausea and occasional vomiting. The cough persisted and was productive of small amounts of white mucous material. Syrup of hydriodic acid gave no relief. There was no hemoptysis, fever or night sweats. Shortly after the onset of the cough, his voice became hoarse, and gradually became worse, until on admission he could only whisper.

Four months before admission he experienced the sudden onset of a sharp, stabbing, substernal and epigastric pain, most pronounced after coughing. It recurred as often as six times a day and was occasionally made worse by deep inspiration. The pain was controlled by medicine that contained a "lot of codeine." Two months before admission he noted progressive weakness of the arms and legs. He had difficulty in keeping his balance and in walking and fell on an average of four times daily. There was urinary urgency without other urinary symptoms. Shortly thereafter he developed constipation, followed by periods of fecal incontinence, occurring about twice a week. There was no distention or melena. One month before entry he developed exertional dyspnea without orthopnea or paroxysmal nocturnal dyspnea. Two weeks before admission he felt as though he had gone to sleep from the waist down. He attributed this to too much codeine, since after omitting the drug this disappeared to some extent. His chest pain also decreased in severity. Nevertheless he was forced to give up his job. His appetite had remained "perfect," but there was a weight loss of 30 pounds in the six weeks preceding entry. He developed several boils.

Physical examination showed a moderately cachectic, slightly dyspneic man who coughed occasionally and spoke in a whisper. The skin was dry. There were a large ecchymotic area over the right knee, and an area of redness, swelling and ulceration over the left wrist. A fluctuant furuncle was present on the left hand. The tongue displayed a coarse tremor. The gag reflex was active. The trachea deviated slightly to the right. There was slight dullness below the angle of the right scapula. An inspiratory friction rub was heard in the right axilla. The diaphragmatic excursion was limited. The left border of cardiac dullness was 10.5 cm. from the midline in the sixth space. The sounds were of good quality and regular. The pulmonic second sound was greater than the aortic. There was a firm, slightly tender mass in the epigastrium according to one observer, and no masses or tenderness according to another. Rectal examination was negative. Neurologic examination showed hyperactive patellar and ankle jerks, unsustained ankle clonus bilaterally, and weakness of both lower extremities, more noticeable on the right. The upper extremities were also weak. There were atrophy and wasting of all extremities. The vibratory sense was diminished in the toes and ankles, and the position sense was absent in the toes. Hypesthesia and hypalgesia extended to the level of the umbilicus on the left, and to slightly lower than this on the right. The touch sensation appeared to be intact. Laryngeal examination was unsatisfactory. The left tip of the epiglottis was ulcerated. The arytenoids and the pyriform sinuses were swollen and reddened. Both arytenoids moved. The cord could not be visualized.

The blood pressure was 168 systolic, 92 diastolic. The temperature was 102.6°F., the pulse 82, and the respirations 28.

Examination of the blood showed a red-cell count of 4,400,000, with 10.5 gm. per cent of hemoglobin. The white-cell count was 11,750, with 78 per cent neutrophils. There was the slightest possible trace of albumin in the urine. The stools were guaiac negative. A blood Hinton test was negative. The vital capacity was 35 per cent of normal. No sputum examination was recorded, but a smear of the gastric contents showed no tubercle bacilli.

X-ray examination of the chest showed a hard, coarse, nodular miliary process involving both lungs (Fig. 1). In addition there were plaque-like areas

of increased density in the central portion of the left chest and in the upper lung fields. At the apices, honeycombing and fibrosis were seen surrounding a few small cavities. The heart was enlarged, and the aorta moderately tortuous. Diaphragmatic motion was limited, and the costophrenic angles were obliterated. A gastrointestinal series and a barium enema were negative. X-ray films of the dorsolumbar spine and pelvis showed a destructive process involving the inferior aspect of the body of the fourth dorsal vertebra and the upper aspect of the body of the fifth dorsal vertebra, with involvement of the disk. In the anteroposterior view there was a questionable soft-tissue mass surrounding these vertebras. No other evidence of a destructive process was seen. A lumbar puncture gave an initial pressure of 270 mm. of water; 10 cc. of clear colorless fluid was withdrawn, the final pressure being 110 mm. The fluid contained 47 red cells per cubic millimeter, but no white cells. The total protein was 63 mg. per 100 cc. The gold-sol curve was 0000122100. The level at which the needle was inserted is not stated in the record, but there was no evidence of blockage.

The temperature remained about 103°F. The patient became more confused and delirious, and died on the eleventh hospital day.

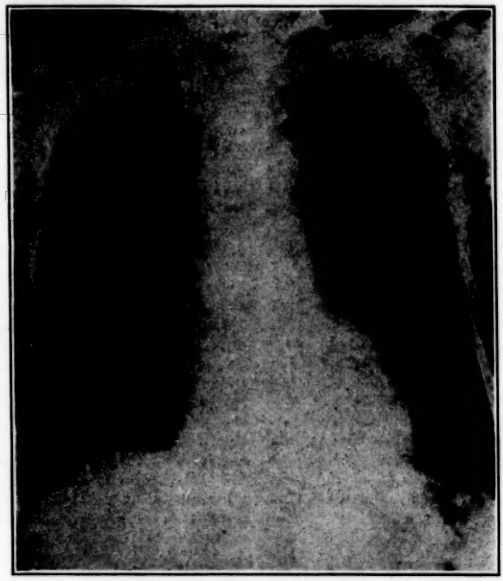

FIGURE 1. *Roentgenogram of Chest.*

DIFFERENTIAL DIAGNOSIS

DR. MAURICE FREMONT-SMITH: This is the case of a sixty-three-year-old man who had apparently been in good health until ten months before entry, at which time he developed cough and hoarseness. Bronchiogenic carcinoma is the first thing to think of when at this age a man's illness begins with cough. He might have had a primary bronchiogenic carcinoma with metastases into the other lung and with a metastatic process in his spine, causing cord changes. Against this is the fact that it is very unusual for a metastatic carcinoma in the lung to form a cavity. Such an explanation would also leave out entirely the changes in the larynx, and if one takes those into consideration the other possibility, which seems by far the most likely, is tuberculosis, which not infrequently becomes active in old age.

This patient apparently had widespread tuberculosis of both lungs and a metastatic tuberculous process in the spine, with a Pott's abscess and laryngeal tuberculosis. He could, however, have had primary laryngeal carcinoma with metastases or primary carcinoma anywhere in the body with metastases. It should be noted that intrinsic carcinoma of the larynx — that is, carcinoma of the vocal cord — does not metastasize rapidly and the

metastases do not occur below the clavicles. Extrinsic carcinoma of the larynx, like any other carcinoma, can metastasize to any part of the body.

The fact that this man had an ulcer on the epiglottis is greatly in favor of tuberculosis. If this process was tuberculous, it is surprising that the patient did not have pain on swallowing and that pain in the larynx was not mentioned.

It is worth while to emphasize two things before going on with the differential diagnosis. In the first place, one is apt to forget that pulmonary tuberculosis can start with hoarseness and not with cough. Secondly, just as we have had impressed on us during the last few years that chronic edema of the legs is not always cardiac, and that a large proportion of patients have edema from other causes, frequently from varicose veins, so too in dealing with chronic dyspnea one is not apt to realize that the dyspnea may come not from the heart but from other trouble in the thorax.

This man also had injury to the cord. Manifestly the pyramidal tracts were involved, with increase in the reflexes and a little clonus, as well as the posterior tracts, with sensory disturbance. The thing that disturbs me is that the muscles of all the extremities were said to be atrophic. The patient could have had atrophy of the legs from the cord injury, especially if the anterior-horn cells were injured by compression. To explain the atrophy of the hands a cervical lesion must have existed, or one would have to premise a generalized disease, such as myotrophic sclerosis, which is farfetched.

Did the boils indicate that there was a secondary staphylococcal blood-stream infection on top of the primary infection, which I believe was tuberculosis? I have gone ahead without looking at the x-ray films and may have to modify some views when I see them.

DR. LAURENCE L. ROBBINS: There is a rather sharply defined mottled process completely involving both lungs. I am not at all sure that I can be positive about the presence of cavities. With this type of process it is a rather difficult decision to make, because numerous superimposed miliary nodules, when taken all together, give an impression of cavities. Certainly there are areas of rarefaction that do suggest small cavities. If there are cavities, I should have expected them to be higher in the right upper lobe.

The films of the spine show destruction and compression of the bodies of the fourth and fifth thoracic vertebras. The disk spaces are not well visualized and there appears to be a surrounding soft-tissue mass.

DR. FREMONT-SMITH: Is it fair to ask whether this picture in the lungs was miliary tuberculosis on top of old tuberculosis of the lung?

DR. ROBBINS: It is hard to be sure that there was an old tuberculous process. It is a fair question to ask, but I do not see how I can answer it. There are certain things, such as a thickened pleura, that may be the result of an old process. The miliary process can be due to several different things from the x-ray standpoint.

DR. FREMONT-SMITH: How about silicosis?

DR. ROBBINS: It might be, but it is atypical. Miliary malignant disease can give a similar x-ray picture.

DR. FREMONT-SMITH: Would you say that it could not be miliary tuberculosis?

DR. ROBBINS: No; that is probably the commonest condition to produce such an appearance.

DR. FREMONT-SMITH: I think that the evidence, including the laryngologic examination, the destructive process in the spine, the soft-tissue mass and the x-ray picture, is in favor of a diagnosis of tuberculosis. The sputum was not examined. The gastric contents were said to be negative. I am rather dubious about the value of gastric contents unless the material is put into a guinea pig, in which case one gets a reasonably accurate diagnosis. That should always be done in a case of probable pulmonary tuberculosis that is not diagnosable by sputum examination. I shall rest my case on the diagnosis of tuberculosis.

DR. BENJAMIN CASTLEMAN: Dr. Means, you saw this patient, will you give us your impression?

DR. J. H. MEANS: Our line of reasoning followed much the same course as that of Dr. Fremont-Smith. We were confronted with a spinal lesion, — compression of the thoracic cord with certain neurologic manifestations resulting therefrom, — and this peculiar lung lesion, with fever. We thought that it was either cancer or tuberculosis, but we did not know which. I tried to pin down the radiologist, but did not succeed. I asked him the following questions: "Can you say definitely that the spinal disease is or is not tuberculosis? Can you say definitely that the spinal disease is or is not malignant? Can you say definitely that the lung lesion is not miliary tuberculosis?" He wrote in answer to all my questions, "No"; but he did favor tuberculosis.

DR. FREMONT-SMITH: Might I ask Dr. Kubik to say a word about my comment on the neurologic findings — that is, how to account for the atrophy of the arms and legs.

DR. CHARLES S. KUBIK: There is definite evidence of cord compression, because of the changes in the leg reflexes and the sensory impairment below a certain level, but I do not believe that we know enough about the atrophy in the arms to be able to say anything about it. That might have been due to the generalized weight loss.

DR. JOST MICHELSEN: Dr. Robbins, do you think the involvement of the disk is in favor of tuberculosis rather than of malignant disease?

DR. ROBBINS: Yes, if I could be sure the disk was involved. A study of that area of the thoracic spine is particularly difficult because of the curvature,

and I am not sure that it is not simply a process of overlapping shadows rather than of active destruction of the disk.

Clinical Diagnosis

Carcinomatosis of lung and spine?
Miliary tuberculosis?

Dr. Fremont-Smith's Diagnoses

Miliary tuberculosis, involving lungs, spine and larynx.
Healed pulmonary tuberculosis.

Anatomical Diagnoses

Miliary tuberculosis of lungs, spine, meninges, larynx and kidneys.
Healed pulmonary tuberculosis.

Pathological Discussion

Dr. Castleman: The autopsy on this man showed a widespread miliary tuberculosis, with a cavity 4 cm. in diameter in the right upper lobe. There was tuberculosis in practically every organ in the body. The fourth and fifth dorsal vertebras, with the intervening intervertebral disk, were involved in a large tuberculous abscess. We were not sure on gross examination whether there was actual invasion of the meninges, but microscopically there is not only involvement of the meninges locally but also involvement of the ependyma of the ventricles, apparently an ascending infection. There was tuberculous ulceration of the larynx.

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COMPARATIVE VALUES

We Americans, with our mixed racial strains, our varied hereditary characteristics drawn from many lands and many ethnologic types, have attained at least one common factor — acquired, perhaps, from an environment that has been overly generous to us. We are generous to others, particularly if a call is made in a way to appeal to our open, warm-hearted, somewhat erratic and at times exceedingly sentimental emotions. If anyone tries to take what belongs to us, we fight at the drop of a hat; but if the emotional floodgates are opened, we give it away. This characteristic is simply illustrated by the old story of the tough character and the flower girl: "Don't cry, little girl. I'll buy your — — violets."

The journalistic gentry learned long ago to pluck the pulsing heartstrings of their public. Crime may go unpunished and injustice may pile unnoted upon injustice, but let some columnist mention the fact that a cripple needs a wheel chair or a veteran requires a wooden leg, and the checks float down like a kindly Christmas snowstorm. The need must be specific and emotionally presented, the beneficiary must be an individual with a personality of sorts, but the response is hundredfold, if it is only a new wig that is requested.

Publicity (or propaganda, if you will) is one of the most powerful instruments that we possess, and a great trust — to use it well and wisely — is put into the hands of those who guide it.

We have seen recently an example of its effectiveness, regardless of how wisely or unwisely it was in this case directed, or whether it was initiated in the best interests of the public. A child suffering from an admittedly incurable chronic nephritis (presumably nephrosis) has had life maintained, or at least has been treated, by the administration of large quantities of blood plasma, the fluid for lack of which many an American soldier may be doomed to die this summer unless the American public is reawakened to its duty. A Boston newspaper, taking up the cause of the child, has obtained enough plasma from local donors to guarantee, it is said, some prolongation of life for the patient.

If journalism will now turn its considerable powers toward obtaining enough blood donors for the Red Cross to make up the deficit of plasma that threatens the effective treatment of our wounded soldiers and sailors, we shall congratulate it most wholeheartedly on the gesture it has made in behalf of the child.

TRENDS IN PNEUMONIA MORTALITY

Most physicians are greatly impressed by the improved outlook with respect to pneumonia. This favorable impression is derived from the better prognosis in individual cases of bacterial pneumonia under modern chemotherapy. Some recent studies, however, indicate that the trend in pneumonia mortality may be changing for the worse, although

it is hoped that these changes will be only temporary.

A recent survey by the United States Public Health Service[1] indicates that since the summer of 1937 pneumonia mortality has markedly declined. An average of the mortality rates for the five-year period 1938–1942 compared with that of the five preceding years showed a decline of approximately 40 per cent, and the decline occurred in all geographical sections of this country. The mortality from influenza and pneumonia for a group of ninety cities in the United States, however, was higher in the third and fourth quarters of 1942 and the first quarter of 1943 than it was in the same quarters of the three preceding years.

Epidemics of minor intensity occurred in five of the eight winters since 1935. Three of these epidemics — (1935–1936, 1936–1937 and 1940–1941) — were practically nationwide. The epidemics of the winters 1938–1939 and 1939–1940 were confined to four or five geographical sections of the country.

An increase in pneumonia mortality was also noted in the latter months of 1942 and the early months of 1943 among the industrial policyholders of the Metropolitan Life Insurance Company.[2] The Metropolitan statisticians noted a sharper than usual rise in the death rate from pneumonia during the winter of 1942–1943, which was much higher than the rise in the corresponding months of the previous year. They believe that this was due chiefly to an increase in the virus or atypical pneumonias, which fail to respond to sulfonamide drugs. They also noted that a large proportion of the fatal cases of the virus pneumonia occurred among young persons. Thus, in 36 per cent of the deaths from this type of pneumonia the patients were between fifteen and forty-four years of age, as compared with the usual figure of 18 per cent. Their data indicated that pneumonia during this period was two or more times as frequent in the Army as in the preceding year and that in some defense areas pneumonia was more than three times as frequent early in 1943 as it was in 1942. In spite of all this, the mortality was still 35 per cent lower than in the first quarter of 1938–1939.

Another interesting review of the public-health and economic aspects of pneumonia was recently published by workers of the Equitable Life Assurance Association of the United States.[3] They compared experience among a large group of industrial employees in the pre-sulfonamide years 1935–1937 with that for the period from January 1, 1939, to June 1, 1942. Most striking was the reduction in the case fatality rate in pneumonia from an average of 20.8 to 3.9 per cent in this short space of time. In addition there was a decrease in the total duration of illness from the modal (most frequent) period of thirty-eight days in 1935 to twenty-seven days in 1941. According to their calculations the lives of twenty-five thousand workers were saved annually, and in addition the loss of a million working days was prevented as a result of the shortening of the period of illness. These authors noted that the incidence of pneumonia increased appreciably during the period of study. They believe that factors such as congestion in industrial areas incidental to the war effort might have been responsible for this increase.

It is well known that deaths from pneumonia increase during periods when influenza is epidemic. Such an increase in pneumonia deaths was associated with the widespread epidemic of influenza in 1940–1941, although this increase was not of alarming proportions. Although the general upward trend of pneumonia mortality during the first part of 1943 did not continue throughout the year,[4] another increase did occur during the latter part of the year as a result of the prevalence of influenza. In New York State, excluding New York City, the number of pneumonia cases reported for the week ending January 1, 1944, was 982.[5] For the week ending January 2, 1943, only 397 cases were reported, and this compares with the 1938–1942 average for the similar period — namely, 358 cases. The reporting of cases of pneumonia is, of course, not accurate and is not required in many states. There is no doubt, however, that the number of primary pneumonias in Massachusetts has increased — perhaps in a similar proportion. In the large hospitals in Boston the great majority of these have been pneumococcal lobar pneumonia.

Whether further increases in pneumonia deaths will occur apart from the epidemic rise remains to be seen. At any rate these recent observations should dispel the feeling of complacency that has

been engendered by the individual successes due to improved therapy. Facilities are still available for pneumococcal typing in Massachusetts, but physicians are not availing themselves of these facilities to a sufficient extent. Many of the recent cases were of great severity, and a significant proportion of them were suitable for combined chemotherapy and specific antipneumococcus serum therapy. Physicians may well benefit from a greater use of the bacteriologic facilities that the Commonwealth and various communities offer to aid in the proper therapy of pneumonia.

References

1. Gover, M. Influenza and pneumonia mortality in group of ninety cities in United States, August 1935–March 1943, with a summary for August 1920–March 1943. *Pub. Health Rep.* **58**:1033–1061, 1943.
2. Recent increase in pneumonia mortality. *Statistical Bull., Metropolitan Life Insurance Company* **24**: (April) 7-9, 1943.
3. Ungerleider, H. E., Steinhaus, H. W., and Gubner, R. S. Public health and economic aspects of pneumonia — comparison with pre-sulfonamide years. *Am. J. Pub. Health* **33**:1093–1102, 1943.
4. Comparative data on causes of death among industrial policyholders. *Statistical Bull., Metropolitan Life Insurance Company* **24** (September), p. 11, 1943; (October) p. 11, 1943; (November) p. 11, 1943.
5. *Health News.* New York State Department of Health, January 10, 1944.

MEDICAL EPONYM

Schilder's Disease

This eponym refers to a form of encephalitis first described by Dr. Paul Schilder (b. 1886), while a teaching assistant of the Royal Psychiatric Clinic in Leipzig, in a paper entitled "Zur Kenntnis der sogenannten diffusen Sklerose: Über Encephalitis periaxialis diffusa [Contribution to the Study of So-called Diffuse Sclerosis: Encephalitis periaxialis diffusa]," which was published in the *Zeitschrift für die gesamte Neurologie und Psychiatrie* (**10**:1-60, 1912). A portion of the translation follows:

> There is a diffuse affection of the white substance of the hemispheres in children that we are justified in regarding as a disease entity on the basis of characteristic macroscopic and microscopic findings in the brain. I propose for it the designation "encephalitis periaxialis diffusa."
>
> The clinical picture of this disease is extremely variable. It follows a course which sometimes resembles that of brain tumor, sometimes simulates multiple sclerosis, or again resembles Heubner's diffuse sclerosis. We may suspect the existence of this disease if symptoms point compellingly to a widespread lesion involving both hemispheres. Attacks with the symptomatology of multiple sclerosis running a rapid course in youthful patients will likewise bring our disease to mind. The disease is a fatal one, with little tendency to remissions.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

TREASURER'S OFFICE

The bills for $10.00 recently forwarded to all members of the Society cover the regular annual dues ("assessment") for membership in the Massachusetts Medical Society. The insert describing the Postwar Loan Fund is purely informative regarding future plans. The current assessment is *not* for the Postwar Loan Fund.

Eliot Hubbard, Jr., *Treasurer*

DEATH

SPALDING — Fred M. Spalding, M.D., of Brookline, died January 24. He was in his seventy-fourth year.

Dr. Spalding received his degree from Harvard Medical School in 1897. He practiced in Boston for many years and served as an intern and later senior ophthalmic surgeon and consultant to the Massachusetts Eye and Ear Infirmary. He retired from active service in 1924, but returned after the start of the war to give his service as an aid to the war effort. He was a member of the Massachusetts Medical Society, American Medical Association and American Ophthalmological Society. He was a former president of the New England Ophthalmological Society.

His widow, two sons and a daughter survive.

NOTICES

BOSTON MEDICAL HISTORY CLUB

There will be a meeting of the Boston Medical History Club in Sprague Hall at the Boston Medical Library, 8 Fenway, on Monday, February 21, at 8 p.m. Dr. Louis E. Phaneuf will speak on the subject "J. Marion Sims — Father of Modern Gynecology."

All interested persons are cordially invited to attend this meeting.

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, February 15, at twelve noon.

Dr. Brainard F. Conley will discuss the Wagner–Murray–Dingell Bill. This proposed legislation (known as Senate Bill 1161 and House Bill 2861) has provoked much discussion in medical and hospital associations and is of interest to every physician.

Physicians are cordially invited to attend.

SUFFOLK CENSORS' MEETING

The censors of the Suffolk District Medical Society will meet for the examination of candidates at the Boston Medical Library, 8 Fenway, on Thursday, May 4, 1944, at 4:00 p.m. Applications must be received not later than February 15.

NEW ENGLAND PEDIATRIC SOCIETY

There will be a meeting of the New England Pediatric Society on Wednesday, March 8. The clinical presentation will be held at the amphitheater of the Children's Hospital, and all other events at Longwood Towers, Brookline.

Program

4:00	Clinical Meeting: Presentation of cases by members of the Children's Hospital Staff.
6:30	Refreshments.
7:00	Dinner.
8:00	Annual meeting.
8:15	Neurosurgical Problems of Childhood. Dr. Franc D. Ingraham.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine will be held at the Hotel Kenmore, Boston, on Wednesday, February 16, at 8 p.m. The topic for discussion will be "The Technic and Results of the Kenny Treatment." Miss Dorothy Fredrickson will discuss and demonstrate the Kenny technic. A council meeting will be held at 6 p.m., followed by an informal dinner in the Empire Room at 6:30.

All members of the medical profession are invited to attend this meeting.

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